VOL. 32 APRIL 1956 NO. 4

BULLETIN

OF THE NEW YORK ACADEMY OF MEDICINE

Original Articles by

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Transcription of a Panel Meeting

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Weiss, A., and Steigmann, F.: Amer. J. Med. Sc. 227:184 (Feb.) 1954.

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Manriott, M. J. L.: Editorial, Annals of Int. M. 40:820 (April) 1954.

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Batterman, R. C.; Dettraff, A. C., and Ross, C. A.: Circulation 3:201 (Feb.) 1952.

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1. Busse, E.A.: Treatment of Rheumatoid Arthritis by a Combination of Cortisone and Salicylates. Clinical Med. 11:1105 (Nov., 1955).
2. Roskam, J., VanCawenberge, H.: Abst. in J.A.M.A., 151:248 (1953).
3. Coventry, M.D.: Proc. Staff Meet., Mayo Clinic, 29:60 (1954).
4. Holt, K.S., et al.: Lancet, 2:1144 (1954).
5. Spies, T.D., et al.: J.A.M.A., 159:645 (Oct. 15, 1955).

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*Tronstein, A. J.: J. Invest. Dermat. *13*:119, 1949.

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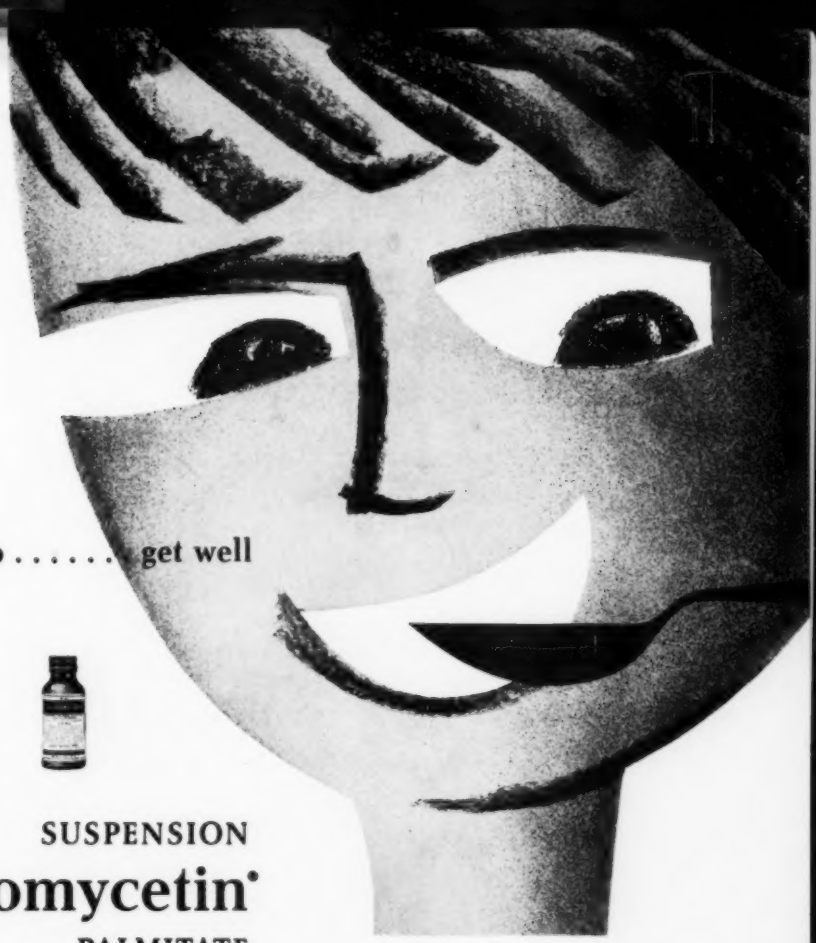

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1. Johnston, R.L.: J. Indiana St. M.A. 46:869, 1953. 2. McHardy, G., and Browne, D.: Southern M. J. 45:1139, 1952.

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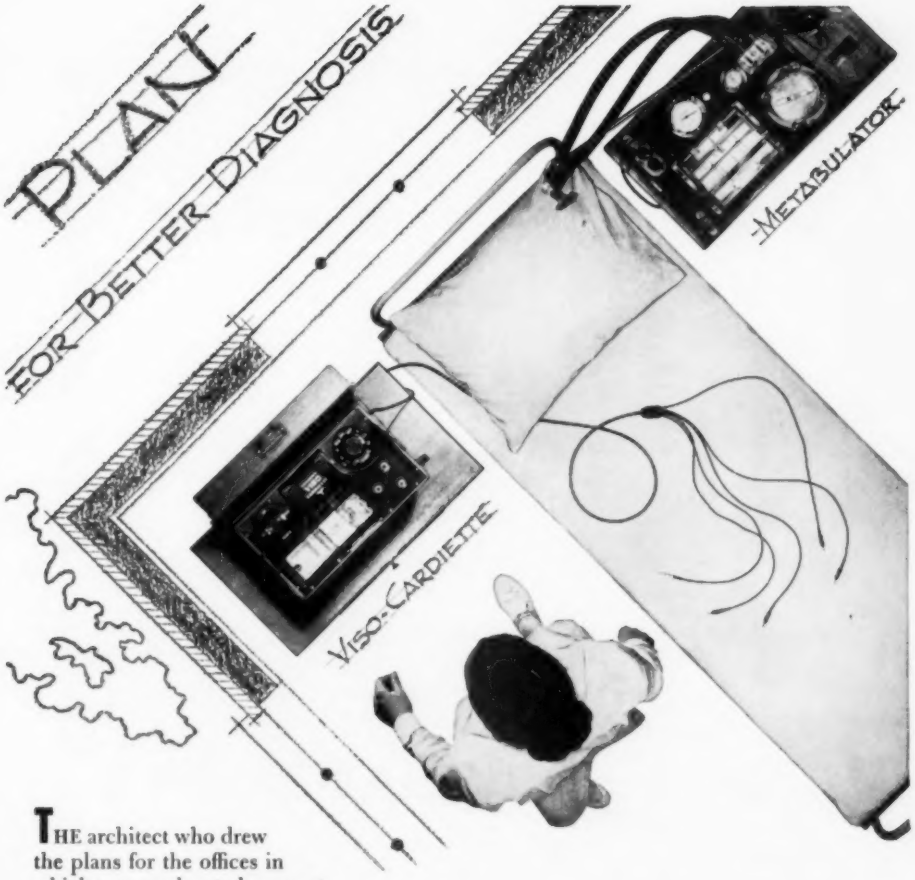

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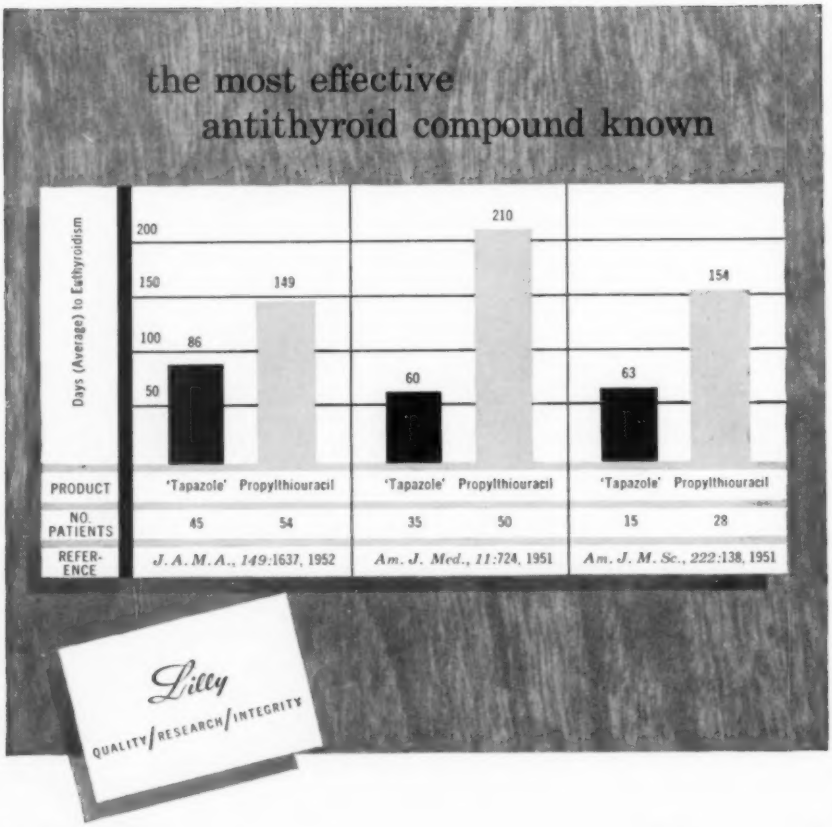

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AUTHORS ALONE ARE RESPONSIBLE FOR OPINIONS EXPRESSED IN THEIR CONTRIBUTIONS

ROBERT L. CRAIG, *Editor*

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BULLETIN OF
THE NEW YORK ACADEMY
OF MEDICINE

VOL. 32, NO. 4 APRIL 1956

ANNUAL REPORT OF THE PRESIDENT*

EDWARD J. DONOVAN

President, The New York Academy of Medicine

IT HAS been the custom for many years for the President to report annually on the state of health of the Academy and on the successes or failures in carrying on its many functions. In the main, the report submitted tonight is a summary of the work done by the five Standing Committees and their various subcommittees, the work of the Sections, the Library,—in fact, all of the important activities in which the Academy has participated in 1955. We are happy to report that the Academy has enjoyed a healthy and successful year, made possible largely through the efforts and cooperation of its Fellows.

COMMITTEE ON MEDICAL EDUCATION

Since the Academy concerns itself primarily with education at the postgraduate level, it seems proper to begin with the report of the Committee on Medical Education. This is one of the larger committees

* Presented at the Annual Meeting of The New York Academy of Medicine, January 5, 1956.

whose chairman this year was Dr. Irving S. Wright, with Dr. Robert L. Craig as Executive Secretary. This Committee has had a busy year and, among other things, arranged the Twenty-Eighth Annual Graduate Fortnight which had as its topic, *Problems of Aging*. The material presented at the Fortnight was of outstanding quality. The clinical, as well as the psychological and socio-economic aspects of the aging process, were discussed thoroughly at evening lectures, including three memorial lectures, the Ludwig Kast, the Carpenter and the Harlow Brooks. These lectures were supplemented by panel meetings, hospital clinics, and a scientific exhibit. This Committee, in cooperation with the Committee on Public Health, the Sections on Medicine, Pediatrics, Neurology and Psychiatry, and the New York Pathological Society, arranged the scientific programs of the monthly Stated Meetings of the Academy. It also provided the programs for the Friday afternoon Monthly Panel Meetings on Therapeutics for the General Physician, which as heretofore, have been well received again this year. It has, in addition, provided a series of basic science lectures for the resident staff of five hospitals in upper Manhattan. These courses have been popular and were presented in rotation at the various hospitals. A Medical Research Forum program presented in January was successful and abstracts of eight papers on original research problems presented at this meeting were published in the Bulletin. Monthly publication of the Grey Folder which announces the Academy programs is also one of the duties of this Committee. During 1955 the Committee awarded one Bowen-Brooks Scholarship in the amount of $2500 to the resident surgeon of one of the large hospitals in the city, for a year of study abroad.

The Editorial Board of the Bulletin

The Academy Bulletin, published monthly under the direction of the Editorial Board, has continued to maintain its high standards. Many requests have been received during the past year for permission to quote or abstract articles or to republish complete papers appearing therein. During 1955 the Bulletin was distributed monthly to 3065 Fellows of the Academy in all categories, and 353 copies were sent in exchange for other journals for the Academy Library, 244 of which were foreign journals. There are now 1,601 subscribers to the Bulletin, 318 of these in foreign countries. The entire Editorial Board deserves

great praise for the success of the Bulletin which requires the expenditure of many hours in its preparation.

Committee on Sections

This Committee concerns itself with all matters relating to the twelve Academy Sections and particularly to their scientific programs. It is composed of a Vice-President of the Academy, designated by the Council as Chairman, the Chairman and Secretary of each Section and the Executive Secretary of the Committee on Medical Education. The Section meetings constitute the greatest contribution of the Academy in continuing medical education for the practitioner, investigator and student. Through the cooperation of the Committee on Sections and the Committee on Medical Information another series of recorded lectures were broadcast weekly during 1955 over Station WNYC–F.M., on the program *For Doctors Only*.

Committee on Medical Information

This Committee is one of the most active groups in the Academy and it performs many functions. It is responsible for the dissemination of medical material to the lay public and for the editing and revision of manuscripts for publication in lay periodicals. It also acts as a liaison agency with and as a source of reliable information for the lay press. It also serves innumerable other functions that relate to medicine and the general public. During the past year the Committee suffered the loss, through illness, of the services of its Chairman Dr. Frank McGowan who had worked so diligently until he became ill. We are happy to report that Dr. McGowan is now greatly improved in health and we are eagerly looking forward to his early return. Dr. Thomas Peightal was appointed Acting Chairman during Dr. McGowan's absence. The Executive Secretary, Dr. Iago Galdston, has, as always, presented a wealth of material for the consideration of this Committee. The Bureau of Medical Information has received and responded to approximately 12,500 inquiries during the past year, 2100 of these inquiries came from the press, 4500 from the medical profession, 2500 from lay individuals and about 3000 from various organizations.

Twenty-eight press releases were issued by this Committee concerning activities of the Public Health Committee, Committee on Medical Education and various other Academy activities such as the Hermann

M. Biggs Memorial Lecture, the Salmon Memorial Lectures, the Graduate Fortnight, Lectures to the Laity, etc. The Committee has been called upon to review 170 manuscripts submitted by numerous lay publications in various parts of the United States. One year ago, this Committee initiated a series of articles written by Academy Fellows and published in the magazine *Better Living*. It is estimated that these articles were presented to a reading audience that numbered in the millions and have been greatly appreciated. They have been reproduced in book form for distribution in schools, women's clubs and other civic organizations. *The Better Living* series is being continued this year and a new series of articles is being projected to deal with pregnancy and childbirth.

The twentieth series of Lectures to the Laity was completed during this year and a new series initiated entitled *Medicine and Anthropology*. This latest series marks something of an innovation in the development of Lectures to the Laity. We are indebted to Dr. Paul Fejos, Fellow of the Academy and President of the Wenner-Gren Foundation for Anthropological Research, Inc., for his aid in the organization of this series and for the financial support of the Wenner-Gren Foundation in the presentations. In connection with this new series, the Committee published a brochure giving a resumé of the achievements of the Lectures to the Laity, since their organization 20 years ago. The Academy wishes to express its thanks to Dr. Harold Brown Keyes, now a Vice-President of the Academy, and Chairman of the Subcommittee on Lectures to the Laity, for his efforts in making this series so successful.

The annual Eastern States Health Education Conference, under the chairmanship of Dr. Herbert Wilcox, was held here on April 21st and 22nd and was devoted to the theme *Goal Oriented Health Education*. These meetings were exceptionally well attended.

A symposium, arranged by the Institute on Medical History, on *The Impact of the Antibiotics on Medicine and Society*, held June 2, 3, and 4, was a distinguished achievement. We are most grateful to Chas. Pfizer & Co., Inc. and to the Wenner-Gren Foundation for the generous financial support of this Institute. A large number of distinguished contributors drawn from the principal medical-history, research and pharmaceutical groups in the United States took part in this program. The transactions of the Institute will be published shortly.

The annual Press-Radio Dinner sponsored by this Committee, held on May 23, was attended by 31 Committee members and Academy officers, while 24 guests representing the press, radio and various publishers were also present.

The Committee on Medical Information assumed leadership in organizing a radio program on Mental Health, broadcast over Station WNYC as a contribution to the nationwide "Mental Health Week" program. A report on the analysis of the findings of the Perinatal Mortality Study was also issued to the press.

The FM program, *For Doctors Only* over station WNYC has also been continued during the year and from this, two developments are noteworthy: 1) The creation of the Graduate Medical Faculty of The New York Academy of Medicine which includes the Chairman and Secretary of each of the twelve Sections. This Faculty is to serve as advisor to the FM Committee in the organization of its program. 2) Arrangements have been completed with the British Medical Association to organize a series of lectures on British Medicine, this series to be included in our own FM program. This Committee has also continued the broadcasting and the publication of *Cancer Alerts* as part of our FM Radio Program. This project has been supported by the New York City Cancer Committee. The Academy wishes to express its most sincere appreciation to Dr. Norton Brown for his splendid work as Chairman of the Subcommittee on FM Programs and for the financial support that he has obtained in its behalf.

Another undertaking of the Committee on Medical Information has been a pilot study on "Whither Medicine" which will be an assessment and an interpretation of the current trends in medicine, medical research, medical education and practice in their various ramifications. As a derivative of this pilot study may come a full project on this topic.

The Transactions of the Conference on Morale held in the fall of 1954 are being reviewed by the Committee and soon will be published. The Committee has published two volumes and is in the process of completing a third one. The volumes published are entitled: *Society and Medicine*, and *Better Health Through Better Living*. The volume in process of publication is: *Ministry and Medicine in Human Relations* representing transactions of conferences held in 1950 and 1952.

Committee on Public Health

In addition to its numerous other duties the Committee on Public Health has undertaken projects of national as well as local importance on request of individuals and groups in charge of such problems. I would like to emphasize briefly four of these projects.

1. *Control of Narcotic Addiction:* At the request of Dr. Frank B. Berry, Assistant Secretary of Defense (Health and Medical Affairs), the Committee on Public Health rendered an opinion on a Congressional joint resolution proposing new measures for the control of narcotics. This resolution was introduced in the Senate last year by Senator Frederick G. Payne and co-sponsored by 42 other Senators. While the resolution died in Committee the request for study was made in anticipation of future action. The resolution dealt with four aspects of narcotic addiction and in the treatment of three of these the Committee was in complete accord. The fourth feature of the bill, i.e., the penalties of twenty years' imprisonment, death or life imprisonment for those who in any way transferred narcotic drugs to persons under 21 years of age, was unreservedly condemned. In the opinion of our Committee severe penalties mean little or nothing when measured against potential profits of illegal distribution or inner craving for the drug. The Committee then formulated a four point program for the management of drug addiction, based upon the concept that drug addiction is a disease. The Committee also emphasized that treatment and rehabilitation would not only rescue those already addicted but would help prevent new addiction. Briefly, it was recommended that addicts be permitted to obtain drugs at low cost under Federal control in conjunction with treatment. This report was transmitted to President Eisenhower, to the Department of Defense, and the Chairman of the Interdepartmental Committee on Drug Addiction.

2. *Problems Relating to Autopsies:* Another problem of great importance studied by this Committee related to solution of the many difficulties associated with the performing of autopsies. For solution, these difficulties require the adjusting of relationships and cooperation between hospital pathologists and the Medical Examiner's office, as do also the problems which arise between hospital authorities and funeral directors. The Committee on Public Health organized a confer-

ence to which representatives of all groups were invited and where the problems were frankly discussed and practical suggestions for solution advanced.

3. *Problems in Medical Service in City Prisons:* A third project of great importance, medical service in New York City prisons, was studied at the request of the Commissioner of Correction, Judge Anna M. Kross who, upon taking office, reported that the New York City prisons were being run as custodial institutions with practically no program of medical treatment or rehabilitation. During the 14 years preceding the appointment of Judge Kross as Commissioner, the department lost many of its specialized staff for medical, nursing, psychiatric and social service work as well as its vocational training and classification personnel. In addition to this state of affairs, the prison population had increased greatly,—with a cell capacity of 4200, the average census was 5700. This task was undertaken by a subcommittee of ten members of our Public Health Committee who visited four institutions and confirmed the findings as outlined by Judge Kross. This Committee after careful study recommended complete reorganization of the entire service, pointing out that the fundamental needs were a larger medical staff, perhaps with the addition of practical nurses, enlargement and modernization of medical facilities including the outpatient clinics and reestablishment of a secretarial and office staff which had become virtually nonexistent.

4. *Changes in the Classification and Compensation of Medical Personnel of the Department of Correction as Part of its Career and Salary Plan:* While the Committee was occupied with the survey of medical service the Department of Correction also requested a review of the proposed changes in classification and compensation of medical personnel as set up for the new City Department of Personnel as part of its career and salary plan. Corrective methods were suggested by the Committee.

The Committee on Public Health, one of the most effective committees of the Academy, with Dr. F. Randolph Bailey as Chairman and Dr. Harry D. Kruse as Executive Secretary, has had a very busy year. Its members spend many hours working out the numerous problems which fall to this group and the Academy is most grateful to the Committee for its numerous accomplishments during 1955.

Committee on Library

This Committee is composed of 18 members elected by the Fellows, with Dr. Samuel W. Lambert, Jr. as Chairman and the President and Director of the Academy as ex-officio members.

The Library, our most prized possession, has had a most satisfactory year under the direction of our able librarian, Miss Janet Doe and her staff. An innovation, that of holding open house for the new Fellows, was tried for the first time this year and proved so successful that it has now become an annual event. The Fellows who were admitted during 1954 were invited by Miss Doe and her staff to meet the members of the Committee on Library, the Academy's officers and executive staff at a party held in the Library on January 2, 1955. After visiting the various departments and learning what resources the Library had to offer, refreshments were served and a very pleasant time was enjoyed by all. Many of the new members spoke of how interesting and beneficial their tour of the Library had been. It is planned to have a similar party on January 17, 1956. The new Fellows will receive invitations and we hope that they will attend.

During the past year the Library has received several legacies,—one of $15,000 from the estate of Dr. John Dorning, another of $930 from the estate of Mrs. Pauline M. Mandelbaum, and another of $12,217 from the estate of Dr. Felicia A. Robbins. Such gifts are not only most useful but they help to maintain the Library on the high plane it has achieved.

We are always proud of the Library exhibits which are placed in the main lobby of the Academy building from time-to-time. Major exhibits in the Library have included: "The Geographic Distribution of Disease," "The Impact of Antibiotics on Medicine and Society," "Early Japanese Medical Books," and the "Development of Attitudes Toward Old Age."

There were several additions to the Rare Book Collection, probably the most outstanding of which was a manuscript on parchment written about 1450 by Roger Marshall, physician to Edward IV of England, dealing with surgery and therapeutics of the time. Its purchase was made possible by a gift of $1000 from the Friends of the Rare Book Room and by $2500 contributed by individuals chiefly through the efforts of Dr. Samuel W. Lambert, Jr. This manuscript is a notable

acquisition and a valuable addition to our collection of early English texts. The "History of Medicine" series, published under the auspices of the Library, has added to its list item No. 12. This is Volume I of *Theodoric's Surgery*, written about 1267 A.D. and recently translated from the original Latin by Dr. Eldridge Campbell and Mr. James Cotton of Albany, New York. The second volume is being prepared for publication.

The Committee on Library joined in an effort to enlist support in Congress for a budget item to provide funds for the building plans of the Armed Forces Medical Library in Washington. The present quarters erected in 1887 are deplorably inadequate for the housing of what is probably the finest medical book collection now in existence.

It is interesting to note that the census of readers in our Library has decreased in the past decade. The reader census ten years ago averaged about 65,000 per year whereas now it is about 39,000 yearly. The reason for this decrease is quite obvious and is due to growth and expansion of university libraries to the point where they are now able to provide adequate working libraries for their staffs. Material which they do not have is still available in the Academy Library which means that although our readers' census has decreased, the Academy Library, second in size only to the Armed Forces Library, must not only have the material for a working library but must also have available the more unusual material requested from time to time by the medical public. An adequate staff must also be maintained to provide such service.

To maintain a library of the first order requires not only constant support from Academy Fellows but from the public as well. Over 50 per cent of our readers are non-medical people coming from industry, management, business, the entertainment field and other areas of mass communication. Adequate support from this non-medical segment of the public has not been forthcoming and should be vigorously sought.

Committee on Admission

The Committee on Admission, although mentioned last on the list this evening, is one of the most important of our committees and carries great responsibility in interviewing and selecting the prospective candidates for Fellowship in the Academy. With Dr. Bret Ratner as Chairman, this Committee has done outstanding work this year and

I wish to take this opportunity to express the Academy's appreciation to them.

Board of Trustees

Acknowledgment should be made of the arduous and conscientious labors of the Board of Trustees who have wisely conserved and invested the Academy's capital assets. These labors, seldom noted and infrequently acknowledged, make possible all of the other activities of the Academy which I have related to you this evening. To Dr. Shepard Krech, Treasurer, and to Dr. Orrin S. Wightman, Chairman of the Board, and to Mr. Arthur A. Eberle, Comptroller, go the thanks of the entire Fellowship.

In the same vein many thanks are due to our able Director, Dr. Howard Reid Craig, whose devotion to the work of the Academy is well known to all of us,—no hour is too late, no task too difficult for him if it in any way concerns the welfare of the Academy.

Conclusion

The New York Academy of Medicine is one of the most unique institutions of its kind in this country. Backed by a tradition of 109 years it has kept pace with changing concepts not only in clinical medicine but in the basic sciences as well, and perhaps equally important, with the changing socio-economic environment. It is interesting to observe the expanding role of the Academy in community and public affairs, and the increased demands put upon it for consultation services by governmental and community agencies and by business and industry. My report to you tonight is sufficiently adequate evidence of this phenomenon but I respectfully urge that we solicit increasing financial support of these functions from those extra-medical groups which benefit from the resources of the Academy.

The past year has been a most pleasant one for your President who has received the utmost cooperation from everyone. It has been a great privilege for me to work with such a splendid group of medical men and women as are the 3000 Academy Fellows who spend so many hours on the various committees, boards, sections, etc., with no other recompense than the satisfaction of a job well done. I wish to express my most sincere gratitude to each and every one of them.

CITATION AND PRESENTATION OF THE ACADEMY PLAQUE* TO MALCOLM GOODRIDGE, M.D.

ASA LIGGETT LINCOLN

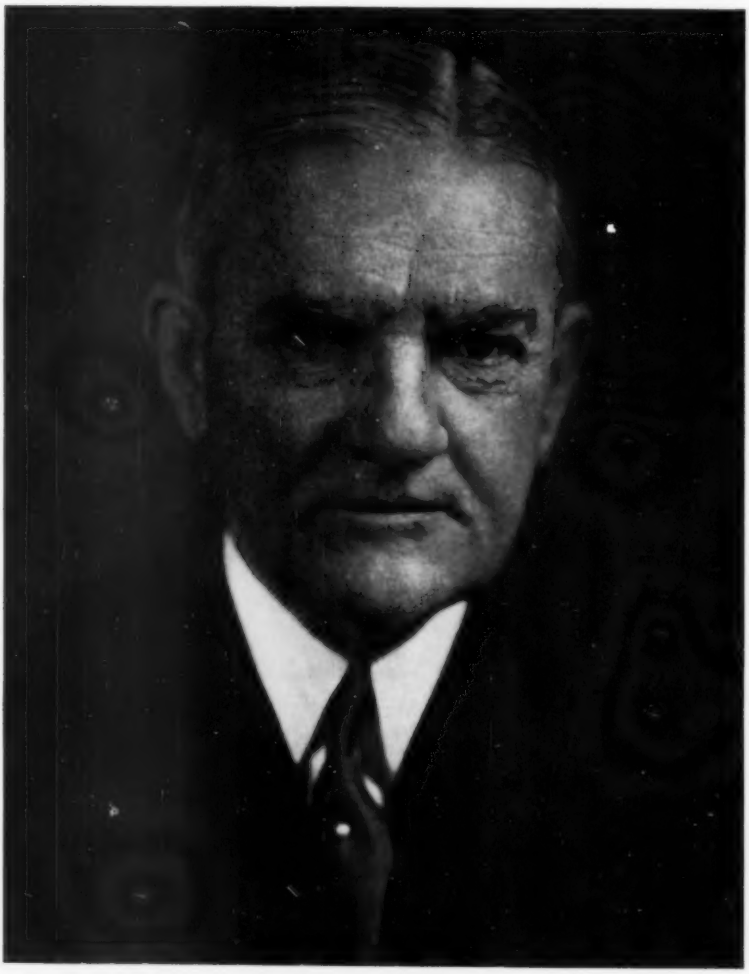
Professor of Clinical Medicine, Cornell University Medical College;
Associate Attending Physician, The New York Hospital;
Trustee, The New York Academy of Medicine

THE strength and vitality of any institution or organization can only be measured by the combined loyalty, devotion, labor and vision of the men of which it is composed. Emerson in his essay on Self-Reliance wrote, "An institution is the lengthened shadow of *one* man"; but The New York Academy of Medicine is the lengthened shadow of many men of good heart, good courage and good will. In this it has been blest.

It is the purpose of the award of this Plaque, which I hold in my hand, to recognize, even in a small way, unusual and outstanding contributions to the life of the Academy. No finer example of devoted service, of strength of purpose and long standing loyalty to this institution can be cited than is exemplified by Malcolm Goodridge. A Fellow of the Academy for 50 years,—dynamic, decisive, wise, he, during his four years of presidency of the Academy, guided the affairs of the Academy through the difficult years just prior to and immediately following our entry into World War II. Faced with institutional financial problems, he mobilized the Fellows and the lay public in a successful effort to weather the uncertain hazards of the early war years. He directed his efforts toward the community problems of those years with understanding, calmness and wisdom, but with great industry.

For eight years previous to his presidency, Dr. Goodridge served on the Committee on Public Health Relations. Following his term of

* Presented to Dr. Goodridge (in absentia) at the Annual Meeting of The New York Academy of Medicine, January 5, 1956.



MALCOLM GOODRIDGE, M.D.

office he returned to that Committee for two more years and in addition served as a member of the Board of Trustees for five years, 1943 through 1947. In addition, he was Vice-Chairman of the Committee on Academy Activities.

In 1942, the Council of the Academy authorized the appointment of a committee "to be informed on the nature, quality and direction of the economic and social changes that are taking place now and that are clearly forecast for the immediate future; to define in particular how these changes are likely to affect medicine in its various aspects; to determine how the best elements in the science of medicine and its services to the public may be preserved and embodied in whatever changed social order may ultimately develop." This Committee became known as the Committee on Medicine and the Changing Order with Malcolm Goodridge as its Chairman. Under his able guidance this group of almost fifty physicians and laymen labored for almost five years and brought out twelve published reports which marked a milestone in the reorientation of medicine in relation to the economy in which it lives and functions. This Herculean task was accomplished only through the skill, tact, understanding and perserverance of its Chairman. The Academy will always be indebted to Malcolm Goodridge for his role in this outstanding contribution to modern medicine.

It is only just and right, therefore, that The New York Academy of Medicine bestow this token of recognition and gratitude to one who has served it so well. I, therefore, as a Trustee of the Academy, have the honor and real pleasure to present this Academy Plaque on which is inscribed:

PRESENTED TO

MALCOLM GOODRIDGE

IN RECOGNITION OF

OUTSTANDING SERVICE TO

THE NEW YORK ACADEMY OF MEDICINE

January 5, 1956

CITATION AND PRESENTATION OF THE ACADEMY MEDAL* TO EUGENE FLOYD DuBOIS, M.D.

DAVID P. BARR

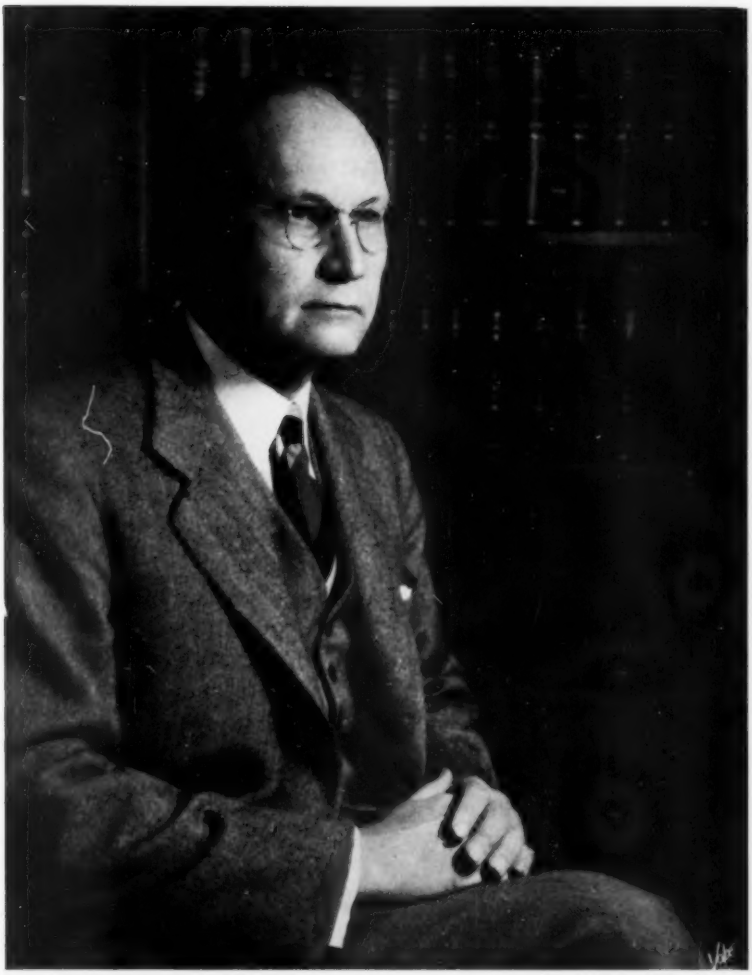
Professor of Medicine, Cornell University Medical College; Physician-in-Chief, The New York Hospital

TWENTY-SEVEN years ago, Dr. Samuel McCullah gave to the Academy funds which made possible the award of a medal for distinguished service in medicine and which was to be given as often as the Council of the Academy might see fit. The medal has been awarded only nine times and always to men of the highest distinction. This evening, the Academy Medal will be given to a man who has blazed new trails in medical science and who has had, in his generation, a unique influence on the development of medical research and education.

Eugene DuBois, whom we honor tonight, was fortunate in acquiring early in his professional life an absorbing interest in a fundamentally important and relatively new branch of medicine. Following his graduation from the College of Physicians and Surgeons of Columbia University and his internship at the Presbyterian Hospital, he went to Europe to study metabolism and nutrition. In 1911, some forty-five years ago, when he returned to New York, he established under the stimulation of Graham Lusk and with the financial aid of the Russell Sage Institute of Pathology a laboratory for investigation of human calorimetry.

This pioneering venture, small and modest at its inception, was destined to have an extraordinary influence on the development of medical science. In a relatively short time there came from DuBois' laboratory contributions on metabolic disturbances in typhoid fever, tuberculosis, malaria, pernicious anemia, leukemia, thyrotoxicosis, nephri-

* Presented at the Annual Meeting of The New York Academy of Medicine, January 5, 1956.



EUGENE FLOYD DUBOIS, M.D.

tis, and cardiac disease. With his cousin, Delafield DuBois, he established a relatively simple formula for the estimation of surface area, now recognized throughout the world as basic to the study of human nutrition and metabolism. With other associates he demonstrated the physical mechanisms of fever and the applicability of van't Hoff's Law to variations in total metabolism observed in fever. Inferences from this work in calorimetry led directly to remarkable studies and to formulations concerning skin temperature and heat radiation.

The significance of the venture was by no means limited to its scientific contributions. To DuBois' laboratory flocked a notable group of young clinical investigators, men who were destined to be leaders of medicine in our generation. Among them were Francis Peabody, James Howard Means, Joseph Aub, William Sharp McCann, John P. Peters, William H. Olmsted, Edward Mason, Paul Larsen, Soma Weiss, and Samuel Z. Levine. Through them and others, DuBois' influence penetrated most of our medical schools and large teaching hospitals.

This extraordinary influence has been attributable only in part to his mastery of experimental procedure and the intrinsic value of his scientific contributions. Its essence derives from his own character and personality. Inspiration has come to others from his abiding faith in principles of scientific and personal conduct, from his integrity and tolerance, and from his sympathetic understanding of the problems of those about him. His character has influenced behavior of his colleagues. It has also influenced innumerable students who have learned from him lessons of critical evaluation, clear expression, unvarying courtesy, and true humility.

Dr. DuBois' military record in the service of his country is one of remarkable achievement and constant contribution. It has been pursued so quietly and at times so secretly that few have realized its extent or significance. In the fields of submarine warfare and aviation medicine, he is an outstanding authority. For heroism in the conduct of hazardous experiments during the first World War, he received the Navy Cross. His service during the second World War was recognized by Commendation and Ribbon Bar. His contributions still continue, and his association with the military service has been maintained and productive since his retirement from academic posts.

To his innumerable friends, it is a matter of satisfaction that honors have been showered upon him: membership in the National Academy

of Science and the Philosophical Society, Presidency of the American Society of Clinical Investigation, of the Association of American Physicians, of the Harvey Society, and of the Institute of Nutrition.

The Academy of Medicine honors itself in awarding its Medal to this great man. To me as one of his most grateful pupils, it is a source of satisfaction that I can be the bearer of a richly merited award.

With the Medal of the Academy I carry to him this citation:

TO EUGENE FLOYD DUBOIS, PHYSIOLOGIST,
PHYSICIAN, EDUCATOR, PATRIOT

IN RECOGNITION OF HIS FUNDAMENTAL CONTRIBUTIONS TO THE SCIENCE OF METABOLISM AND THE UNDERSTANDING OF DISEASE; OF HIS INFLUENCE UPON THE THOUGHT AND ACTIVITIES OF OTHER LEADERS OF MEDICINE; OF HIS ACCOMPLISHMENTS IN THE DEVELOPMENT OF CLINICAL SCIENCE AND MEDICAL EDUCATION; OF HIS SYMPATHETIC UNDERSTANDING AND ENCOURAGEMENT OF YOUNGER MEN; OF HIS SERVICE TO HIS COUNTRY DURING TWO WORLD WARS IN SOLUTION OF PHYSIOLOGIC PROBLEMS IN AVIATION MEDICINE AND SUBMARINE WARFARE.

HIS LIFE AND WORK HAVE BROUGHT
HONOR TO THE PROFESSION OF MEDICINE.

SOME PHYSIOLOGICAL ASPECTS OF AGING IN MAN*

The Wesley M. Carpenter Lecture†

N. W. SHOCK, Ph.D.

Chief, Section on Gerontology, National Heart Institute, National Institutes of Health, P.H.S., D.H.E. & W., Bethesda, Maryland and the Baltimore City Hospitals, Baltimore, Maryland

ALTHOUGH a precise definition of aging may offer semantic difficulties, it is a concept which all individuals recognize, particularly those who have attained the age of 50. Aging is a biological phenomenon which is common to all living organisms, and hence is a proper topic for investigations in comparative physiology. This evening's lecture will, however, be concerned with a discussion of the physiological aspects of aging in man. Since aging is a process which directly concerns all of us, we are interested primarily in a description of what happens to people with the passage of time. We all know that, with the passage of time, the incidence of disease increases and the probability of dying within the next year or five years is enhanced. This latter fact is illustrated graphically in Figure 1, A and B where the logarithm of the mortality rate is plotted against age. It may be seen that after the age of 40 or 50 years the plots are essentially straight lines with a constant slope.[1] Comparison of the curves for India, where mortality rates are high, with those of the United States,[2] indicates two major points: (a) the slopes of the curves are strikingly similar, and (b) the curve for the United States is displaced to the right. Thus, a given rate of mortality was attained in India at ages approximately 15 years younger than in the United States. Figure 1 B shows a similar relationship for mortality rates in the United States in 1900 as compared with 1950.[3] Here the displacement is approximately five years. These curves serve to illustrate the biological aspects of aging. The fundamental biological problem is to determine the factors that influence the slope of the curves—to find out why there is a systematic increase in the probability of death with increasing age. Changes in position of the mortality

* Presented at the 28th Graduate Fortnight on *Problems of Aging*, of The New York Academy of Medicine, October 12, 1955.

† In memory of Dr. Wesley M. Carpenter.

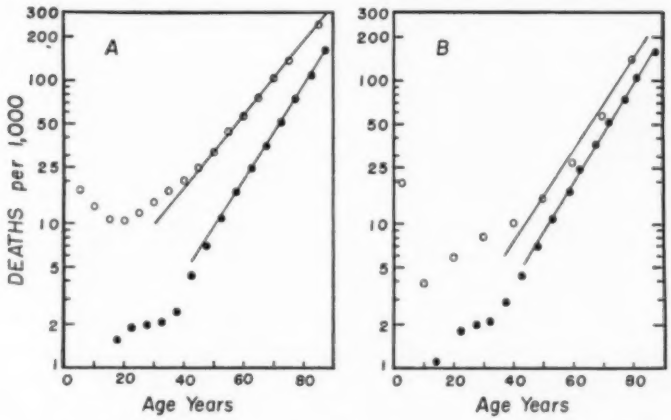


Figure 1—Log total mortality rates plotted against age. A. Comparison of mortality rates for India o—o and the United States •—•[3]. B. Improvement in mortality rates in the United States between 1900 o—o and 1951 •—•[3]. There is a displacement of the curves to the right, with little change in the slopes of the linear part of the curves.

curves, that is, the displacement of the curves toward the right, are influenced by environmental factors such as improved hygiene and the reduction in disease incidence. Consequently, part of the problem of aging is closely associated with the prevention of diseases such as cardiovascular diseases, cancer, arthritis and mental disease. Therefore, to consider aging of man in the "absence of disease" is an abstraction which has little possibility of full attainment. Research on the problems of cardiovascular diseases, cancer, etc. have a direct bearing on problems of aging. However, for the discussion this evening, we shall be concerned primarily with the description of changes which occur in the absence of diagnosable disease states; e.g., changes which at least at the present moment are not regarded as disease. It is well recognized that age changes as identified today may represent states of early pathology and, with a sharpening of diagnostic procedures in the future, many of the observed characteristics may prove to be the early stages of disease. For my own part, I regard aging as the changes which take place in the organism with the passage of time. Consideration of Figure 1 leads to another important generalization, namely, that the probability of death at any age is influenced by what has happened to an individual earlier in life. Thus, studies on aging must take into account the entire

life span, including the periods of growth and development if we are to understand the aging process. Ideally, we should be able to collect observations on the same individual throughout his life span. Practically, we are as yet unwilling to support long term studies of this kind. Hence, we must do what we can to describe the characteristics of different individuals who have reached different points on the curve of mortality. If we could choose sufficient numbers of subjects randomly from the population, it would be unnecessary to exclude subjects with specific disease states. However, most studies must be carried out on already selected populations where the probability of the occurrence of disease is greater than in the general population. Hence, it is desirable to exclude from aging studies those individuals where disease can be identified.

Theories about the nature of aging have existed since our earliest records of history. Unlike other fields of science where a steady progression from a large number of speculative to one or two highly probable main hypotheses may be found, theories of aging can only be catalogued. These theories fall into two major groups: (a) those which regard aging as an inherent property of living matter, and (b) those which attempt to relate aging to impairments in specific physiological systems, of which the gonads have been most popular. Even now, we do not have enough information to choose between the hypothesis that aging is a biological phenomenon inherent in all animals which proceeds even in the absence of disease, or whether aging and death occur only as the accumulation of pathological processes. In the case of the human, the evidence is fairly clear that a good many years of longevity could be added to the human simply by reducing and minimizing the effects of disease. If there is a fundamental biological process which limits life span, surely few, if any, humans have ever approached this ceiling.

Our approach to the problem of aging has been to describe, as quantitatively as possible, changes in physiological functions in individuals who are free from clinical symptomatology of a disease state which would influence the organ system under study. Although the data presented may not meet the rigorous criteria of studies on aging, the data are descriptive of aging people. Furthermore, since we regard aging as a process, it is obvious that we must examine not only older people but also study individuals distributed over the entire life span.

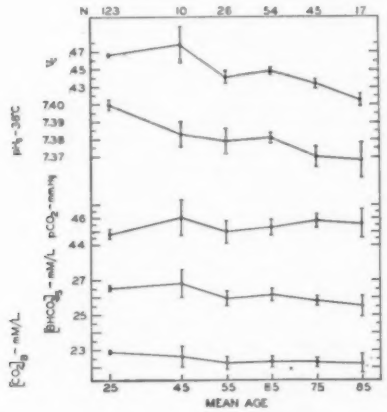


Figure 2—Trends in the acid-base equilibrium of the blood of males with increasing age. Average curves from top to bottom include per cent red cells, serum pH at 38 C., carbon dioxide tension expressed in millimeters of mercury, serum bicarbonate, and blood carbon dioxide content both expressed in millimoles per liter. The vertical lines indicate ± 1 standard error of the mean. From Shock and Yiengst[4] in *J. Gerontology* 5:1-4, 1950. Reprinted by permission.

Thus, in all of our studies, we have attempted to include, within the population tested, individuals ranging from ages 20 to 90.

All of the data, which I shall present tonight, have been taken from studies carried out in the laboratories of the Section on Gerontology. In these studies, we have had, over the past several years, the collaboration of Drs. Luther E. Smith, J. E. Cohn, Dean F. Davies, John H. Miller, David H. Solomon, Leroy E. Duncan, Roger K. McDonald, Morton D. Bogdonoff, Martin Brandfonbrener, Donald M. Watkin, Milton Landowne and Mr. Marvin J. Yiengst. Without the active collaboration and day-to-day operations of experiments by these investigators, this presentation would have been impossible.

Although it is commonly assumed that all physiological processes go down hill as we grow older, our laboratory investigations have shown that this is not always the case. For example, we have found that the regulation of the acid-base equilibrium of the blood does not change systematically with age.[4] Figure 2 shows the average values in 152 men distributed between the ages of 45 and 90 years, compared

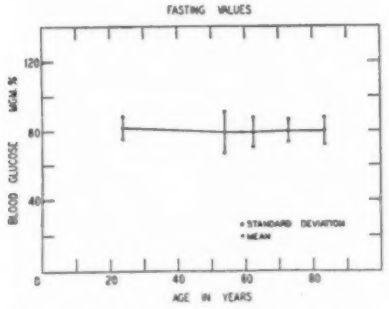


Figure 3—Average fasting glucose level in arterial blood of males. Vertical line indicates ± 1 standard error of the mean. Data from Smith and Shock.[5]

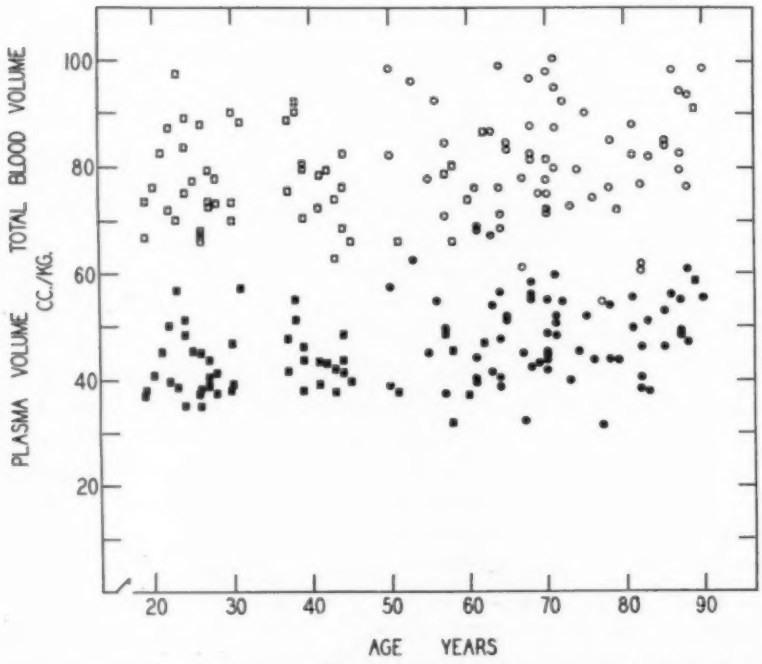


Figure 4—Total blood volumes, cc. per kg. and plasma volumes, cc. per kg. in 105 males. □ total blood volume determinations from Gibson and Evans[9]; ■ plasma volume (Gibson and Evans[9]); o total blood volume; ● plasma volume. From Cohn and Shock.[5] *Amer. J. med. Sci. 217*:388-91, 1949. Reprinted by permission of the publisher, Lea & Febiger.

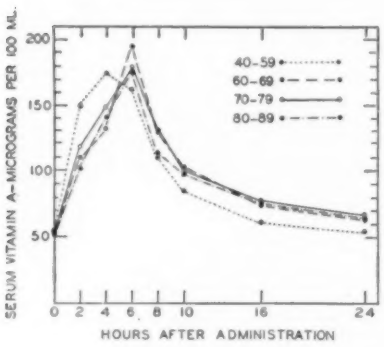


Figure 5—Vitamin A plasma levels in males of 4 age groups following oral administration of 100,000 units of vitamin A.

o - - - - o 13 subjects aged 40-59 years;
o —— o 15 subjects aged 60-69 years;
o ——— o 15 subjects aged 70-79 years;
o - - - - o 15 subjects aged 80-89 years.

From Yiengst and Shock,[10] in *J. Gerontology* 4:205-11, 1949. Reprinted by permission.

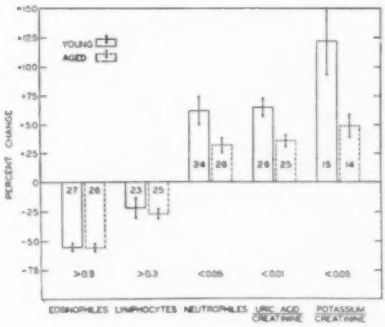


Figure 6—The responses of young and aged men to the intramuscular administration of 18 mg. of ACTH. The ordinate represents the per cent change from basal value during the four hours after ACTH administration. The bar ending each column indicates the mean; the circles indicate the standard error of the mean. The number of cases analyzed is shown within the columns. The probability of the chance occurrence of the observed difference is shown below each pair of columns. From Solomon and Shock,[11] in *J. Gerontology* 5:302-13, 1950. Reprinted by permission.

with observations on 123 students.[5] There is a slight diminution in the average pH of the blood in the older subjects, but the bicarbonate content and CO_2 tension of the plasma are maintained within normal limits. Thus, under resting conditions, the mechanisms available for regulation of acid-base balance are apparently adequate for the task, even in the 90 year old man.

Similarly, the fasting arterial blood sugar level is apparently unaffected by age,[6] as shown in Figure 3. There is, however, some evidence that venous blood sugar levels are slightly increased in the older subjects.[7] Estimates of blood volume, using the Evans-blue dye technique, have been made in 60 carefully selected subjects with results as shown in Figure 4.[8] Thus, elderly individuals, who are free from any clinical signs of fluid accumulation or edema, have approximately the same blood volume per unit of body weight as the young subjects studied by Gibson and Evans.[9]

In Figure 5, a comparison of the changes in blood vitamin A level, following the oral administration of 100,000 units of vitamin A, is

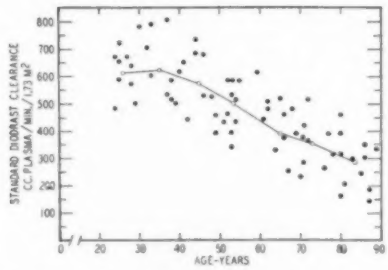


Figure 7—Change in standard diodrast clearance or effective renal plasma flow with age in males. o——o average values cc. plasma/min./1.73 sq. M. body surface area. From Shock,[12] in *Cowdry's problems of ageing*, 3.ed. (A. L. Lansing, ed.). Reprinted by permission of the publisher, The Williams & Wilkins Company.

shown for 126 males between the ages of 40 and 90 years.[10] Examination of this figure shows that, with the exception of an earlier peak response in 40 to 50 year old age groups, along with a somewhat more rapid return to resting values, there is little evidence for any significant differences between the older subjects and the 60 year old group. Thus, age does not seem to be an important factor in determining the absorption of vitamin A.

The eosinophile response to the intramuscular administration of ACTH was not significantly different between our young and old subjects (Figure 6).[11] Significant age changes were observed in the excretory measurements, i.e., the uric acid/creatinine and potassium/creatinine ratios in the urine were lower in the old than the young subjects. In view of the reduced renal function in older people which we have observed,[12, 13] it does not seem safe to ascribe the alterations in excretion to the responsiveness of the adrenal cortex to ACTH. In a number of extensive metabolic balance experiments, we have measured the ability of elderly males to retain nitrogen when placed on augmented protein intake.[14-17] In all of the experiments, we have found that the older individual is just as able to retain nitrogen as the young when offered increased amounts of protein in the diet. Thus, we have a whole array of physiological processes which show similarities, rather than differences, between the old and the young. These results show that, where a number of regulatory systems are involved, equilibrium

may be maintained in the old subjects as well as in the young. This is particularly true when subjects are tested under basal or resting conditions. When a physiological stress is placed upon the organism, the older individual usually shows a greater physiological response and a slower rate of return to basal or resting levels.

There are, however, a number of physiological functions which show definite age differences even under basal or resting conditions. For example, there is a progressive diminution in renal plasma flow with increasing age.[12, 13] Figure 7 shows a scatter plot of values obtained in a series of carefully selected subjects. No subjects with clinical evidence or history of renal disease were included in the series. Subjects were also excluded if they had a blood pressure greater than 140/90. Thus, the changes in plasma flow, as indicated in the figure, represent changes that at least, at the present, can not be regarded as evidence of renal disease. It is important to note, first of all, the wide individual differences, and secondly, the gradual decrement in the mean values beginning at the age of 30 to 40. It may be seen that some of the 80 year old subjects had renal plasma flows as large as the mean value of the 40 year old group. The wide individual differences observed in renal function are equally true in the case of other measurements we have performed. A similar reduction in glomerular filtration rate, as well as the maximum rate of excretion of diodrast, and the maximum rate of reabsorption of glucose, has been found. In fact, the average decrement in all of these functions is percentage-wise about the same; i.e., the reduction is uniform in all of these functions at a rate of approximately 6 per cent per decade. In order to determine whether the vascular bed in the kidney of the aged had lost its functional capacity to respond to physiological stimuli, a series of experiments was carried out on which renal function was measured during the administration of a vasodilator.[18] In these experiments, renal vasodilatation was induced by the injection of 50,000,000 killed typhoid organisms (0.05 cc. TAB vaccine). Results of these experiments are plotted as average curves for the young, middle and old subjects in Figure 8. Following the administration of the renal vasodilator, a gradual increase in renal blood flow was observed in all age groups. On a percentage basis, the increase in flow was as great in the old as in the young subjects. The reduction in filtration fraction, which is apparent for all three age groups, is evidence that the renal vasculature in the old subjects was

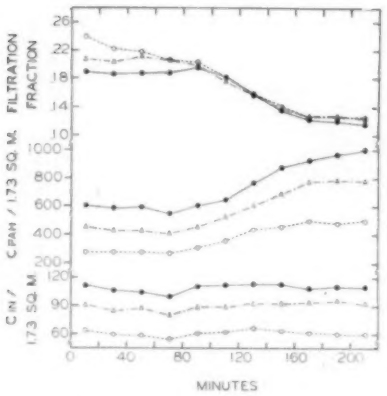


Figure 8—Changes in Cin, Cpah, and FF during pyrogen reaction. Fifty million killed typhoid organisms were injected intravenously at o time — male subjects.

o——o mean value for 14 subjects in O group (70-85 yrs.)

Δ- - - -Δ mean value for 20 subjects in M group (50-69 yrs.)

•———• mean value for 20 subjects in Y group (20-49 yrs.)

From McDonald, Solomon and Shock,[18] in *J. clin. Investigation, 30*:457-62, 1951. Reprinted by permission.

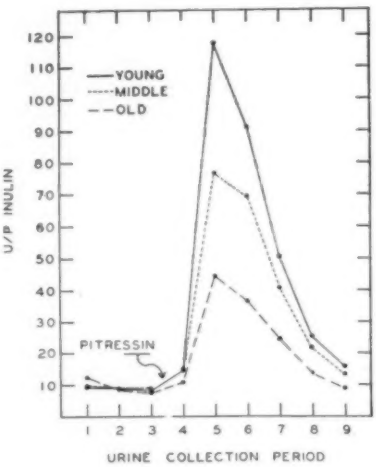


Figure 9—Mean values of U/P inulin ratio for each of 3 age groups before and after the intravenous administration of pitressin. Urine collection periods 1-9 represent 9 consecutive twelve minute periods. Pitressin was administered immediately after the conclusion of period 3. Inhibition of water diuresis is indicated by a rise in U/P inulin ratio. From Miller and Shock,[19] in *J. Gerontology, 8*:446-50, 1953. Reprinted by permission.

capable of responding to the physiological stimulus since this response is not related to the number of functioning nephrons present in the kidney.

Other experiments have shown that with increasing age there is a progressive loss in the ability of the renal tubular cell to perform osmotic work.[19] In these experiments, carefully selected subjects were hydrated and infused with a solution of inulin to permit the estimation of the glomerular filtration rate. Since this substance is filtered at the glomerulus and passes without reabsorption down the tubule, calculation of the ratio of inulin in the urine to that in the plasma offers a measure of water excretion or absorption. After a series of control observations, pitressin (.5 milliunits/kilogram body weight) was administered intravenously. Figure 9 illustrates the average results for groups of young, age 24 to 45; middle aged 46 to 65, and old, 66 to 86

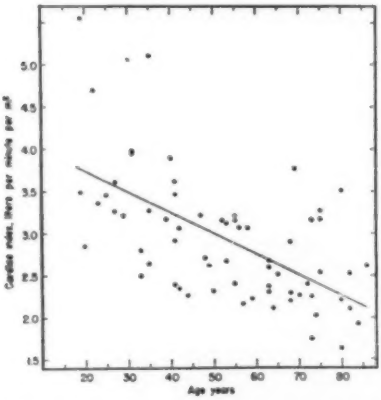


Figure 10—The relation between basal cardiac index and age in 67 males without circulatory disorder. Each point represents the average of 2 measurements in 49 subjects, of 3 measurements in 4 subjects, and a single measurement in 14 subjects. The line indicates the simple linear regression for the data. From Brandfonbrener, Landowne and Shock,[20] in *Circulation, 12*:557-76, 1955. Reprinted by permission of the publisher, Grune & Stratton, Inc.

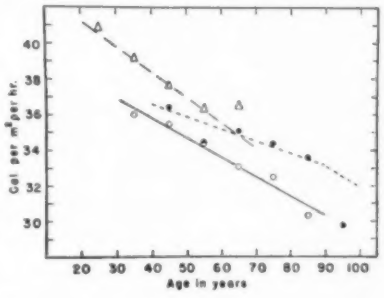


Figure 11—Linear regression of basal heat production of males on age. Mean values by decades are shown as individual points.

Δ——Δ data of Boothby, Berkson and Dunn[21];

•-----• data of Lewis[22];

o——o composite values for subjects (age 30-90).

From Shock and Yiengst,[23] in *J. Gerontology, 10*:31-40, 1955. Reprinted by permission.

years. Although the urine flow during the control periods was slightly less in the older group, there was no significant age difference in the U/P inulin ratios. Following the administration of pitressin, prompt antidiuresis was noted in all three groups as evidenced by a rise in the U/P inulin ratio. It may be seen that the young subjects responded with a marked inhibition of the diuresis when pitressin was administered, in contrast to the aged group where the effect, though present, was greatly diminished in extent.

Using the dye injection technique, we have also been able to demonstrate a significant diminution in the resting cardiac output with increasing age.[20] Subjects for these experiments were carefully screened to exclude any individuals with clinical signs of heart disease. Figure 10 shows the overall change in cardiac output with increasing age. Although a part of the diminution in output can be ascribed to a slight reduction in heart rate with age, and a small proportion can be attributed to a reduction in body size, there remains a significant reduction in stroke index with increasing age.

The gradual fall in basal heat production, per square meter of surface area over the age span of 20 to 60 years, reported by Boothby, Berkson and Dunn,[21] has been projected in setting standards for metabolism at higher ages. However, when older subjects were studied by Lewis,[22] the rate of fall in BMR with increasing age was somewhat less than that predicted from the earlier data. We have determined basal metabolism in 152 males between the ages of 40 and 90 years.[23] The data from our studies, as well as those of Kountz, Chieffi and Kirk[24] are summarized in Figure 11. Although the calculated surface area of individuals diminishes slightly with increasing age, the basal heat production, or oxygen uptake, falls at an even greater rate so that basal metabolism per unit of surface area shows a gradual decline. The rate of decline is almost identical for studies made on residents in old peoples' homes in Baltimore and St. Louis. It is of interest that the rate of decline in basal metabolism was apparently less among the community residing subjects tested by Lewis.

On the basis of the evidence presented, we may conclude that not all physiological processes show a diminution with age, and that those which do, show gradual changes extending over the life span without evidence for any sudden changes at a given chronological age, with respect to the average. This, of course, is not to say that periods of rapid change may not occur in individuals. However, before a definitive answer can be given to this question, it is necessary to have repeated observations in the same individual over his entire life span. Such data are not available at the present time, with the exception of a few subjects who have worked in the field of metabolism and have had estimates of basal metabolism made at various periods in their life span. It is interesting that the decrement per ten year period in most of these six individuals was approximately the same as that reported in our mean curves.[25] It may also be concluded that there are wide individual differences in the physiological changes that take place with age, i.e., there are factors other than age which play a large role in influencing decrements within an individual. This is indeed a hopeful sign and one which offers opportunity for maintenance of physiological status in older people if we can identify the other factors of the environment which are producing decrements in function.

How then can these age changes be explained? On the basis of histological evidence, we know that, with increasing age, there is a reduction in the amount of active protoplasm in a good many organs.[26] Thus,

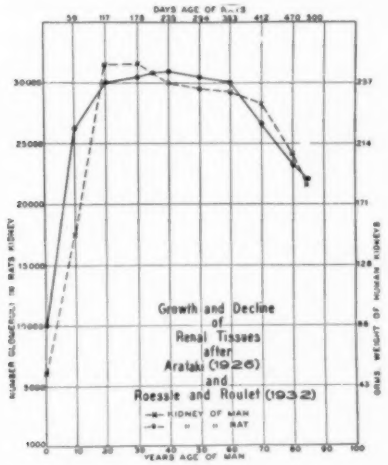


Figure 12—The growth and decline of the renal tissues after Arataki[27] and Roessle and Roulet.[28] From article by Oliver,[29] in *Cowdry's problems of ageing,* 3.ed. (ed. by A. I. Lansing). Reprinted by permission of the publisher, The Williams & Wilkins Co.

for example, the number of nephrons which could be counted in the kidney in the rat[27] and the kidney weight in man[28] show a gradual reduction with age (Figure 12).[29] Similar reductions in active protoplasm have been reported in a variety of other tissues. What we really want to know is how much of the age changes which are observed in the functional capacities of the total animal can be explained on the basis of a simple loss of tissue or protoplasm and how much must be ascribed to a reduced function in the protoplasm remaining. This question can obviously be answered only if we have some index of the amount of protoplasm in the body. Because of the increase in fat and water and other substances that replace active protoplasm as the animal ages, the use of body weight, or calculated surface area, is not an adequate index. In view of the findings of Lowry and Hastings[30] for example, that the intracellular water content of protoplasm is constant and does not change with increasing age, it is possible that the determination of the amount of intracellular fluid in the intact animal might offer a better index of the amount of protoplasm than either weight or calculated surface area. Although methods for estimating the extracellular water content in the intact animal leave much to be desired, the utilization of

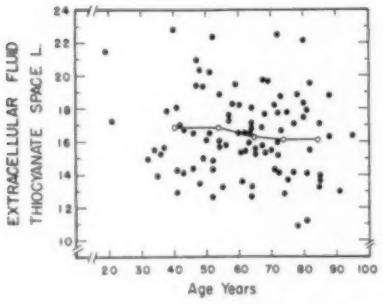


Figure 13—Relationship between extracellular fluid space (thiocyanate space) and age in males.

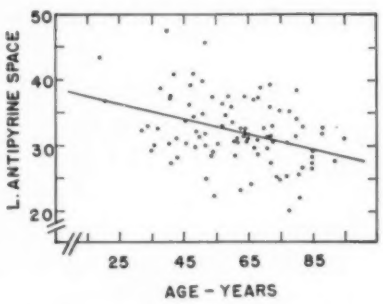


Figure 14—Age changes in total body water in males (measured by antipyrine space).

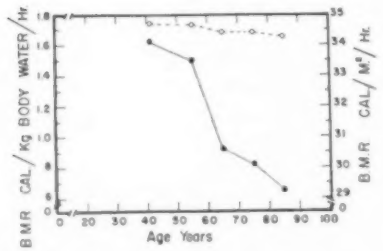


Figure 15—Age changes in basal heat production and basal oxygen consumption in males.

o - - - - o basal heat production, cal./M²/hr.

•———• basal oxygen consumption, cc. O_2/liter antipyrine space.

When expressed in terms of body water, the age change in basal metabolism disappears. Data from Shock.[32]

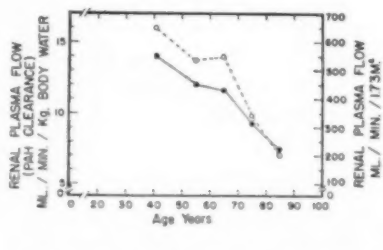


Figure 16—Renal plasma flow (cc./min.) expressed in terms of total body water (antipyrine space). The age decrement in renal function remains.

antipyrine for the determination of total body water offers some promise.[31] We have made simultaneous estimations of thiocyanate and antipyrine spaces in a series of individuals between the ages of 20 and 90 years.[32,33] In these experiments, an intravenous infusion containing 1 gram of antipyrine and 1 gram of thiocyanate ion in 50 millimeters of physiological saline was administered to each subject under basal conditions, following the withdrawal of the control blood sample. Additional bloods were drawn at ½, 1, 2, 3, 5 and 7 hours after the beginning of

the infusion. Each of the fluid spaces was calculated by estimating the concentration at zero time by extrapolating the straight line obtained when the logarithm of the concentration was plotted against time. The average values for extracellular water or thiocyanate space did not change with age (Figure 13), but there was a significant reduction in antipyrine space or total body water (Figure 14).

Since basal metabolism determinations were done on the same group of subjects on whom the fluid spaces were estimated, it was possible for us to calculate the basal oxygen uptake per kilogram of body water. When these calculations were made, it was found that the basal oxygen uptake per kilogram of body water, did not change significantly with age (Figure 15).[33] Thus, if we are willing to accept either total body water or intracellular water as an index of the amount of functioning protoplasm in the intact animal, we are forced to conclude that the oxygen uptake in functioning cells in old animals is no different from that in young animals under resting conditions; i.e., the age decrement in basal oxygen uptake may be explained completely on the basis of reduced amount of functioning protoplasm. However, not all of the changes, described above, can be attributed to a loss of total body protoplasm alone. For example, renal function measurements were made in 63 of the subjects on whom determinations of fluid spaces were made.[34] In these subjects, calculations of renal function, per unit of body water, did not remove the reduction apparent with increasing age. This, of course, does not say that the reduced renal function may not be due to a reduction in the number of functioning units in the kidney. It simply says that, if this is true, the rate of decline in the amount of renal tissue is greater than the overall decline in the total body (Figure 16).

As is often the case, these experiments raise more questions than they answer. For example, we would like to know to what extent the total oxygen uptake in the animal is related to the oxygen uptake of specific tissues. Such questions can obviously be answered only in animal experiments where sacrifice is possible. Although there are studies on the oxygen uptake of tissues from lower animals, the data are controversial and it cannot be said that a reduction in oxygen uptake has been demonstrated in the tissues of older animals.[25] Although it seems reasonable to suppose that there are metabolic changes in a cell that must precede its disintegration and disappearance, we must admit that this is one of the challenges for future research.

Thus, it is clear that, although a part of the diminution in physiological function of various organ systems may be ascribed to the loss of functioning tissue, some functions show changes which cannot be accounted for on this basis alone. The problems of aging offer a challenge to future research. First of all, we need to identify quantitative alterations in a specific organ system performance. Secondly, we need studies of the integrated performance to find out how organ systems work together to meet bodily stresses. The application of new research techniques, to characterize the responses of old and young animals, offers an opportunity for increasing our understanding of aging in the human animal.

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NUTRITIONAL PROBLEMS OF ADVANCING AGE*

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Two important health problems of advancing age are obesity and atherosclerosis. Our Department of Nutrition at Harvard has active researches in both areas and we feel both problems are basically nutritional in their origin. I should like to tell you briefly about some of our recent findings in these studies. I am sure you must all be aware that most of what I shall relate is the work of a number of hardworking colleagues and graduate students, and not my own. Also that by telling only of our work I do not mean to imply that others are not actively working on these problems. But my time is limited, it's easier to tell you about our own work and obviously we think it important or we would be doing something else.

We have done a great many studies of various aspects of obesity during the past ten years in both man and a number of different types of animals. Generally my colleague, Dr. Mayer, has directed the animal studies and Dr. Trulson has had charge of the studies with man.

A simple study which has only recently been prepared for publication involves the role of non-caloric sweeteners in overweight subjects. This may have some practical interest to some of you.

Two groups of individuals were questioned about their use of non-caloric sweeteners and artificially sweetened products. Group I was composed of 147 obese individuals who were subjects in a three-year follow-up study of the effectiveness (or really lack of effectiveness) of various reducing programs. Group II consisted of 100 obese patients referred to the nutrition clinic of the Peter Bent Brigham Hospital in Boston and who were followed a relatively short time.

Thus there were 247 obese subjects. Of this number, 105 were using or had used non-caloric sweeteners and/or artificially sweetened prod-

* Presented before the 28th Graduate Fortnight on *Problems of Aging*, at The New York Academy of Medicine, October 12, 1955.

TABLE I.—THREE YEAR WEIGHT STUDY

147 Obese Subjects	*Non-Caloric Sweeteners*	
	Yes	*No*
No. of Subjects who Lost Weight	47	49
No. of Subjects who Gained Weight or had the Same Weight	25	26

ucts. To attempt to determine the effectiveness in weight reduction of the use of non-caloric sweeteners, the data from the follow-up study on Group I were analyzed with respect to weight loss and the use or non-use of non-caloric sweeteners. About one-half of these subjects were using or had used these products. The subjects' weights before the instigation of the weight reduction program and at the time of the three-year follow-up study were tabulated. The percentage of the initial per cent overweight lost or gained was determined. Sixty-five per cent of both groups (users and non-users) had at some time during the three-year period lost some weight. Usually this was during the first two months of starting to reduce. No difference in weight loss between those that had used non-caloric sweeteners and those that had not was apparent. The results are summarized in Table I.

A study was made of the length of time non-caloric sweeteners were used and weight loss. It was found that the length of time the products were used did not alter the weight change pattern.

Of the 100 obese patients in the hospital clinic group, 33 were users of non-caloric sweeteners. The weight loss of these subjects while using non-caloric sweeteners and artificially sweetened products was not evaluated because of the short time the individuals had been on the reduction regime and because the accuracy of the reported weight loss would depend upon the reliability of the patients' memory and their wish to be accurate. However, of the 33 patients who had used the product 11 believed they lost weight and had received definite help from employing such products and 22 said they had either gained weight or their weight had remained the same.

An attempt was made to find out if the degree of overweight was associated with the use of non-caloric sweeteners. Of the total number

of 247 subjects, 67 were 50 per cent or more above their desirable weight, and of these, 36 used non-caloric sweeteners, and 31 did not. No relationship between degree of overweight and the use of non-caloric sweeteners was evident.

Generally the use of non-caloric sweeteners by the obese subjects was limited to sweetening tea and coffee and occasionally cereal, dessert, and fruit. The actual use of artificially sweetened foods by this group was small as compared with a group of diabetic patients we were also studying.

By and large, weight reduction regimes when considered from the long-range point of view are quite unsuccessful. Many aspects of obesity are yet unknown or little understood. Certainly little is known of methods of motivation that are effective over an extended period of time. It is obvious that there is no one key to the problem of obesity. The use of non-caloric sweeteners and artificially sweetened foods when considered on a group basis is not of particular value in a reducing program. However, it is well to remember that it is the individual who is losing weight, not the group. Therefore, if one out of four or five individuals is helped to some extent, the use of non-caloric sweeteners may have a place in the diets of some obese individuals.

The preventive aspects of weight control should be stressed since most attempts at long-term weight control along curative lines have so far failed. The old saying, "An ounce of prevention is worth a pound of cure", is certainly true in the problem of obesity, an important problem in advancing age.

It might be of interest to simply mention a number of specific suggestions which we have evolved as a result of researches in both animals and man and that may be of some practical importance in dealing with this problem in man.

1. Prevention is better than treatment.
2. Early treatment is better than late treatment.
3. Parents should set good examples for their children. If they eat like gluttons, what can you expect of the children?
4. Use the bathroom scales—weekly or monthly and keep a written record of weight.
5. Eat 3 meals a day—a good breakfast—eat in the daytime, not at night.

6. Eat slowly. This allows the blood sugar to rise and satisfy the appetite before it is time for "seconds."
7. Cut down on the total food. It is not necessary to eliminate any single food.
8. Take your choice between cocktails or dessert.
9. If necessary, use "scientific nibbles," not "common nibbles," to help curb your appetite.
10. Mild to moderate daily exercise is helpful.

Please remember these are suggestions not all documented by firm evidence, but they may be helpful to those who have to struggle with an overweight problem.

Next, a few interesting findings related to atherosclerosis, particularly some relatively new and positive findings on the importance of exercise in the disposition of food calories. These studies have been done by my colleague, Dr. Mann, and are being extended largely by Drs. Hegsted, Portman, and Andrus of our Department.

Atherosclerosis is certainly an important problem of advancing age and one where there is a strong nutritional component. Not only is it a problem of advancing age but a problem of middle age as well, and it is a problem which within the last month has received considerable public attention.

The evidence relating the level of the serum lipids to the etiology of experimental atherosclerosis in animals is pretty strong. I believe atherosclerosis has now been produced experimentally in five different species,—the rabbit, chick, dog, rat, and in a primate, the Cebus monkey. The presence of atherosclerosis has been reported in other species, such as the pig, but I am not aware that it has been produced experimentally in any species other than the five I have listed. In all of these it was necessary to find a procedure whereby the serum cholesterol, and the other serum lipids, could be elevated for a certain length of time. There seems to be an intensity and a time factor—the level of the serum lipids and the time they are elevated.

The development of refined biophysical methods for the characterization of serum lipids has not greatly clarified this serum lipid-disease relationship although the new methods have emphasized a lack of correlation between the serum cholesterol and lipoprotein quantities in human subjects which was unexpected in view of the biochemical sim-

ilarities of the two and the close correlations which are found in subhuman animals that have been studied both before and after hypercholesteremia was induced.

We cooperated with the Institute of Nutrition of Central America in a study of the lipid levels of Guatemalan subjects subsisting largely upon vegetarian diets. These researches[1] revealed an unexpected dissociation of the serum beta-lipoprotein and cholesterol levels. These subjects showed low and almost constant cholesterol levels at all adult ages. The levels, which were near 150 mg. per cent for both sexes, of that adult population, are characteristic of North American children. In contrast, the serum beta-lipoprotein levels in the Central American subjects were similar to those of the North American subjects when compared according to age and sex. It became of interest to examine the hypotheses that some characteristic of the environment of the Guatemalans might account for these observations. There were two conspicuous differences between the study groups: 1) The Central Americans were found to eat much less fat than the North Americans. While it has been shown that limitation of dietary fat will often lead to a reduction of the serum cholesterol and serum beta-lipoprotein levels, there has been no evidence produced that this treatment will selectively lower the cholesterol level, leaving the beta-lipoproteins unchanged or even increased as would be necessary to explain the Central American findings. 2) The studies in Central America indicated that while those subjects were thinner than age- and sex-matched North Americans, the Central Americans consumed more food daily in relation to body size. These facts could only mean that high energy expenditures by the rural Central Americans must account for the weight differences. This conclusion was consonant with the vigorous activity required of individuals in that agrarian culture. We were thus led to consider that there might be some favorable effect of muscular exercise upon the regulation of the serum lipids which selectively keeps the serum cholesterol level low.

Other studies[2] we have done with adult American males have indicated that under certain conditions changes in weight affect the serum lipids. Thus, we have shown that a period of weight loss in human subjects will result in a reduction of the levels of serum lipoproteins and cholesterol *but only if these were initially elevated*. Conversely, we showed that a short period of rapid weight gain even if

accomplished on a low fat, low cholesterol diet increased both of those serum lipid components.

We recently completed a somewhat similar, but more elaborate study, to which a vigorous exercise component was added.[3]

Four medical students were engaged to participate in an experiment of ten weeks' duration. The subjects were paid a good wage in addition to their food, and this was the principal initial motivation of three of the men. The fourth, although also paid, was interested in the experiment.

The men were fed at a research diet table during the entire experiment. Food was served by research dietitians who measured the intake of food. The subjects were observed for the first week under these conditions on an *ad libitum* food intake with their usual physical activity and while maintaining their body weights at a nearly constant level. From these dietary measurements the intakes of fat and total calories were computed and averaged for each subject. In the second period which was of four weeks' duration the caloric intake was approximately doubled while the fat intake was kept constant at the control level, about 175 gm. and the subjects were required to maintain their body weights within five pounds of the mean weight during the control period by *strenuous* daily exercise. This was the high energy expenditure period. In the third period of three weeks' duration, the subjects returned to the control level of energy expenditure but the high calorie and constant fat intake continued thus permitting the deposition of body fat. In the fourth and final period of two weeks' duration, the subjects were restricted in food calories with the dietary fat again remaining constant but the exercise was omitted except for that occasioned by their usual academic activity as in the first and third periods.

The large food intakes of the second period were reached by a stepwise increase over a 48-hour period at the beginning of the period in order to give the subjects time to adapt to this great dietary change. During the seven weeks of high calorie intake, the subjects ate three major meals under observation at the research table and in addition took supplementary feedings consisting principally of measured amounts of candy bars, marshmallows and soft drinks. These supplementary meals furnished 25 to 30 per cent of the total daily calories.

The high energy expenditure was accomplished by a rigorous schedule of daily physical training. The subjects spent three hours every

day engaged in vigorous physical activity in a gymnasium. Swimming, basketball and sprinting proved the most useful activities. These activities were supplemented as necessary by cycling and outdoor running.

Blood was drawn in the post-absorptive state at weekly intervals during the experiment and the serum was used for the measurement of cholesterol and of the beta-lipoproteins.

Three subjects completed the regimen in all details. The fourth subject was unable to maintain a constant weight and retired at the end of the second week of high energy expenditure. It may be of interest to mention that the subject leaving the experiment because of excessive weight gain was a tall, lean individual who initially argued that no one could make him gain weight.

The findings clearly indicated that during the high energy period, despite the large intake of calories, there was no essential change in weight, serum cholesterol, or the lipoprotein fraction measured.

These observations indicate that young men consuming high fat diets were able to double their caloric supply without increasing the level of their serum lipids so long as the excess energy was dissipated as exercise. The findings support the concept that serum lipid levels are related to the calorie balance of the body.

The experiment described may represent in a microcosm the nutritional progress of an adult American male. A period in early adulthood of high energy turnover may then be followed by a long period of diminishing physical activity but with unchanging dietary habits. This leads in a variable time to an obese individual at middle age with poor muscular development, with elevated serum cholesterol and beta-lipoprotein levels, though without visible lipemia. More important, there is generally significant atherosclerosis in such a man. The present experiment may have shortened these simulated phases excessively. By not allowing time for the large changes of body inventory, the full effects upon the serum lipids may have been minimized or obscured. There seems little doubt but that significant effects can be produced on both the body composition and the serum lipids in most subjects by these alterations of diet and physical activity.

After middle age, if this hypothesis is true, we have a patient in advancing physiologic age, with atherosclerosis and its many unpleasant complications.

It would be of interest to know whether a larger sample of this

age, or a sample of older subjects, would have shown a similar degree of response. The two subjects studied previously without the heavy exercise component, each of whom responded promptly to positive calorie balance with increases of the serum lipoproteins and cholesterol, were 27 and 38 years of age. The present subjects were in that age group (24 years) where there is anatomical evidence to indicate that atherogenesis is beginning.

The sera of these subjects which were drawn in the post-absorptive state were clear throughout the experiment. The lack of increase either of neutral fat as measured chemically or of low density beta-lipoproteins measured with the ultracentrifuge conforms with the observation that the serum lipid changes which occur with positive calorie balance and adiposity are of the invisible high density beta-lipoproteins. It should be emphasized that visible lipemia in serum obtained in the post-absorptive state is uncommon in subjects of any age and cannot be a necessary development for the development of atherosclerosis.

The subjective responses of these men to the experiment reveal two observations of possible clinical usefulness. While the first days of physical training produced discomforts and fatigue, the men soon experienced a sense of well-being and accomplishment which they considered adequate compensation for their troubles. During the low exercise, weight gaining period which followed, the men continued to eat the excessive food intakes without complaint and even with some relish, but as they grew fat they became sluggish and, in their own evaluation, less efficient in their daily activities. Nonetheless they were complacent in this progress of obesity. The first reaction may mean that physical conditioning is self-rewarding and sufficient motivation in itself, aside from any desirable effects it may have in preventing atherogenesis. The second reaction indicates that dietary habits, even when of a short duration, have high inertias. This tardiness of adjustment of food intake to metabolic requirements may be based on obscure physiological phenomena which are in addition to the contribution made in real life by social customs, culinary artistry and changing values of a pleasurable activity which occur with age.

Conclusion

What does all this mean to the practicing physician who is faced with the real problem of advising his older patients about their diet?

Essentially the older person's food needs do not differ from those of the young. A variety of nutritious foods each day are as important to him now as at any time in his life. Precisely because he is older and his tempo of living has slowed, his digestive system has slowed up a bit too. His caloric needs are lower because he is not so active as in his younger days. He may find small meals more comfortable and satisfying than large ones. Chances are that his dentures are not what they used to be. For this reason he may require foods that are easily chewed.

Sound nutrition for the elderly differs only slightly from that of the younger adult. The principal differences are:

1. Fewer calories, and, because of the need for fewer calories, activity somewhat above the maintenance level should be encouraged. Such activity will also stimulate the peripheral circulation, strengthen bones, and improve gastrointestinal activity.

2. A smaller proportion of calories should be contributed by fat and a larger proportion by protein, though current and future researches may indicate that it is the saturated fats which should be consumed in smaller amounts as distinguished from unsaturated fats.

3. Dietary modifications, necessitated by poor dentures, low income, inadequate cooking facilities and poor appetite are often required.

4. Lastly, and probably most important, physicians and others respond best to disability, disease, deficiency, and distress. We must learn to respond equally well to prevention, protection, preservation, and the improvement of health, both personal and public. For these are the principles which if applied *prior* to advancing age will make that period healthier and happier. And here proper nutrition is of most importance.

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RENAL CALCULI

*Transcription of a Panel Meeting**

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Panel Members

GORDON D. OPPENHEIMER

The Mount Sinai Hospital

GEORGE W. SLAUGHTER

Lenox Hill Hospital

ROBERT M. SPELLMAN

St. Elizabeth's Hospital, Boston, Massachusetts

FRANCIS P. TWINEM

Lincoln Hospital

*Presented at a meeting of the Section on Genito-Urinary Surgery at The New York Academy of Medicine, March 16, 1955.

JAMES J. TOOMEY
Chairman

FREDERICK T. BOND
Secretary

MODERATOR MARSHALL: Although it is probably not necessary to introduce the panel members to you, we shall go through the formality. They are all excellent urologists and have been selected because of studies they have made on renal calculi or because of special interest in this field.

The first is Dr. Francis P. Twinem, the Chief Urologist at Lincoln Hospital. He has been interested in calculous disease for a number of years and has studied recurrence rates. Next is Dr. George W. Slaughter of Lenox Hill Hospital, whose particular reason for being on this panel is that he has developed what appears to be an excellent method for removing staghorn calculi. Dr. Gordon Oppenheimer, of Mt. Sinai Hospital, has been interested in recurrence rates for different kinds of stones and especially in recurrence rates following different types of operations for their removal. The end man in this show is Dr. Robert M. Spellman of St. Elizabeth's Hospital in Boston. He is imported, not only to add a touch of youth, but also because he has made a special study of the Shorr program for the prevention of certain types of calculi.

We decided to have a panel meeting instead of a symposium, because we believe in this way we might cover the more interesting, yet not closely connected, questions and especially a variety of controversial matters that have to do with renal calculi.

Dr. Twinem, considering all the patients with renal stones in the New York area, what percentage of first or original kidney stones are composed principally of cystine?

DR. FRANCIS P. TWINEM: The percentage in one large series was 2 per cent, and this corresponds quite well with other studies. Some records show 1 per cent or less.

MODERATOR MARSHALL: *How frequent are uric acid and urate stones?*

DR. TWINEM: Uric acid stones constitute about 5 per cent.

MODERATOR MARSHALL: *Oxalates?*

DR. TWINEM: We frequently get mixtures of oxalate and phosphate; but considering those that are predominantly oxalate in the ureteral and renal stone group, they constitute about 40 per cent.

MODERATOR MARSHALL: *How about phosphatic stones?*

DR. TWINEM: Phosphatic stones make up most of the remainder, which would be about 53 per cent. These figures, of course, are approximate and they vary in different parts of the world. Patients in southern

Asia have more uric acid stones than occur in the New York area. The figures, too, would be somewhat different for bladder stones.

MODERATOR MARSHALL: *Suppose we consider only recurrent stones, or more properly the patient who has had numerous recurrences, the "stone-former". Do these percentages change, in New York City again?*

DR. TWINEM: Yes, in recurrent stones there tend to be many more phosphatic ones.

MODERATOR MARSHALL: *About how many more?*

DR. TWINEM: There aren't so many of the oxalate stones that recur. The exact percentage, I do not know, but in cases of recurrent calculi we estimate that about three quarters of them are phosphatic. I have never compiled any precise figures on the recurrences alone.

MODERATOR MARSHALL: *What percentage of staghorn calculi are of cystine composition?*

DR. TWINEM: In the series that I studied they were 6 per cent of the staghorn calculi. This is a higher figure than for stones generally because a rather high proportion of cystine stones are of the staghorn type: for instance, in the eight cases of cystine stones that I can recall, four were of the staghorn type.

MODERATOR MARSHALL: *I am a little surprised at that. I hadn't thought of it as being quite that high. Do all cystinurics get calculi?*

DR. TWINEM: No, not by any means. Only about 2½ per cent of cystinurics actually develop calculi.

MODERATOR MARSHALL: *You say that about 6 per cent of staghorn calculi are cystine in type. About what percentage are phosphatic?*

DR. TWINEM: The percentage that are phosphatic is quite high, because there aren't many calcium oxalate stones—at least, large pure calcium oxalate stones. Very few stones that are pure calcium oxalate are of the staghorn type. Although I have no precise figures, my estimate would be that probably more than 80 per cent of staghorn calculi are of phosphatic or at least of various phosphatic combinations; about 20 per cent would be pure calcium phosphate.

MODERATOR MARSHALL: *You have some pictures of a staghorn calculus of cystine. Would you like to show these briefly?*

(At this point Dr. Twinem showed and described a few slides concerning cystine calculi.)

DR. TWINEM: This is a rather unusual case of cystine calculi. I saw this boy when he was 16 years of age. He had a history of having passed

a small stone when he was six months old, and again when he was 14 years old. Here is the picture which we found at the age of 16 (large bilateral calculi). There was much argument as to whether this boy should be subjected to surgery at all, but we did operate upon him. Here is a recent x-ray of this boy, taken 18 years after the operation. He is now 34 years of age, has three children, and is active. He has been treated in a simple manner, being on an alkaline ash diet and taking simple medication as indicated, to keep his urinary pH above seven. On a few occasions he has had renal lavage, but how much good that has done I don't know. For a long time I could find nothing that would cure his urinary tract infection with B. lactis aerogenes. About a dozen different antibiotics were tried but finally Ilotycin accomplished the desired result.

While we are showing slides I shall anticipate things a bit. This slide shows the percentage of recurrences in the opposite kidney where there has been an operation for renal calculus. Here are 102 cases of pyelotomy with three recurrences in the opposite kidney. Also, here are 100 nephrotomies with 28 per cent recurrence in the same kidney but only two appearances of stone in the opposite kidney. When a nephrectomy was done in 48 cases, there was recurrence in the opposite kidney only in two, or 4.2 per cent.

MODERATOR MARSHALL: *Do you think cystinuria tends to run in a family?*

DR. TWINEM: Yes, that is correct.

MODERATOR MARSHALL: *You mentioned the young man had three children. Have any special studies been done on these children?*

DR. TWINEM: No, the children have not been studied. I am just about to take up that matter.

MODERATOR MARSHALL: *Dr. Slaughter, do you agree with what Dr. Twinem has said so far?*

DR. GEORGE W. SLAUGHTER: I do.

MODERATOR MARSHALL: *Dr. Slaughter, what about hyperparathyroidism as the cause of renal calculi? How many of the patients with calculous disease not only have hyperparathyroidism but also have the hyperparathyroidism as the cause of the stones?*

DR. SLAUGHTER: I think hyperparathyroidism is a very *uncommon* cause of urinary calculi. There is much more hyperparathyroidism being verbally tossed about than is actually present in patients having

stones. The minute you mention stones, everyone begins thinking of hyperparathyroidism.

MODERATOR MARSHALL: *Considering the stones in staghorn calculi, what percentage might be the direct result of hyperparathyroidism?*

DR. SLAUGHTER: Not a single one of those whom I have operated upon, except perhaps the most recent one which has not yet been studied in this regard.

MODERATOR MARSHALL: *Dr. Oppenheimer, is your experience about the same?*

DR. GORDON D. OPPENHEIMER: My experience with renal calculi associated with hyperparathyroidism leads me to believe that it is a rare condition, but I do think it may occur in somewhere between .2 per cent and 1 per cent of all cases of renal calculi. This probably depends somewhat on the care with which the cases are worked up.

MODERATOR MARSHALL: *Dr. Spellman, what tests ought to be done in looking for hyperparathyroidism?*

DR. ROBERT M. SPELLMAN: I haven't had experience with hyperparathyroidism but I looked up the excellent paper by Black of the Mayo Clinic which was published in 1953. He reviewed 112 cases of hyperparathyroidism and found that 73 of them developed renal calculi. He didn't distinguish between nephrocalcinosis and renal pelvic calculi. He seemed to believe hyperparathyroidism can be ruled out if two determinations of serum calcium and serum phosphorus levels are normal. He didn't seem much impressed with the 24-hour determination of calcium in the urine, since it is subject to so many variations.

MODERATOR MARSHALL: *Did he make mention of the serum proteins? My understanding is that calcium is partially attached to these proteins. If the serum protein level is not determined you may not get a true picture.*

DR. SPELLMAN: Yes, a significant amount of measurable calcium is combined with the serum protein, so that if you have an abnormal serum protein the determination of calcium alone could lead to significant error. For example, if the serum proteins are low there would be a distinct tendency for the serum calcium also to be low, a situation which could co-exist during the variable phases of hyperparathyroidism.

MODERATOR MARSHALL: It is my impression that the measurement of the 24-hour output of calcium in the urine is a quite valuable diagnostic test, provided the patient is on a standardized diet.

DR. SPELLMAN: This would be laborious as a routine screening test. Certainly, the urinary levels would gain in significance if the patient were on a standard diet, and I would guess that Black also thinks so. He did, however, stress particularly the calcium and phosphorus levels in the serum.

MODERATOR MARSHALL: There are other tests, of course. Dr. Ephraim Shorr, who is here tonight, has been working on this problem for some time and has developed what appears to be a useful test. It is a calcium tolerance test. Our clinical experience with the test is so limited that I, as a urologist, cannot adequately comment upon it. We have searched and tried all sorts of blood tests, yet we find only the rare patient with stones who also has hyperparathyroidism.

Dr. Slaughter, if hyperparathyroidism is corrected will stone formation stop?

DR. SLAUGHTER: I do not think so.

MODERATOR MARSHALL: *What do you think, Dr. Twinem?*

DR. TWINEM: I think it will. I think that there will be less likelihood of recurrence.

MODERATOR MARSHALL: *What do you think, Dr. Oppenheimer?*

DR. OPPENHEIMER: I think that if you would remove all the stones from such a kidney, so that there will be no remaining calculi and if you also remove the parathyroid adenoma, no stones will form in that kidney due to hyperparathyroidism.

MODERATOR MARSHALL: In other words, it really depends a great deal on the status of the kidneys at the time you remove the parathyroid adenoma.

DR. OPPENHEIMER: That is obvious.

MODERATOR MARSHALL: If the kidneys are in good condition, stone formation would stop and that statement is probably 90 per cent true. I have had no great experience but we have had a few such patients.

Dr. Spellman, if renal function has already been affected adversely will renal function improve if the hyperparathyroidism is corrected?

DR. SPELLMAN: I think you must make a distinction between various renal complications of hyperparathyroidism. One of these is nephrocalcinosis and another is renal pelvis stones. Unfortunately, once nephrocalcinosis has reached the phase where renal failure is measurable, then removing the adenoma has only a slight effect on improving renal function. In other words, renal failure then may well continue progressively

to death. Nephrocalcinosis is the most feared complication of hyperparathyroidism.

MODERATOR MARSHALL: In other words, the status of the kidney at the time the parathyroid adenoma is removed has much to do with the future course of the patient. If the kidneys are in good condition, function will usually return and the stones usually won't return. If the stones are still there, and especially if the renal parenchyma is severely affected as in nephrocalcinosis, there is likely to be steady progression to renal failure.

Dr. Slaughter, in the causation of staghorn stones, what do you think is the role of obstruction-infection? Stones in the bladder are primarily the result of obstruction (plus the residual urine) and infection. How many staghorn stones form in the kidneys on this same general basis?

DR. SLAUGHTER: A small percentage. I think that infection, rather than causing it, usually follows the stone formation.

MODERATOR MARSHALL: *What percentage of staghorn stones occur bilaterally?*

DR. SLAUGHTER: In my experience, about 20 per cent.

DR. SPELLMAN: In Dr. Slaughter's paper reviewing 80 cases of dendritic calculi, 16 were bilateral. We recently reviewed a series of 18 cases of staghorn calculus and three of these patients had bilateral stones. Dr. Edward Brady of Bellevue Hospital found three of 19 were bilateral. Accordingly, the 20 per cent figure is probably correct.

MODERATOR MARSHALL: *Dr. Twinem, do you have any facts, theories, or opinions as to why one kidney may develop a staghorn calculus while the other kidney does not? We usually think that what circulates through one kidney circulates through the other, and investigators have spent much time talking about what is going into the renal machinery to produce the particular stony exhaust.*

DR. TWINEM: In the case of phosphatic stones, which are in the majority, I think that local factors are important. With cystine stones, I think there must be a definite metabolic factor. There is a much higher percentage of bilateral cystine stones than of bilateral phosphatic stones. Some local factors must be involved, because only about 14 per cent of stones are bilateral. If stone formation were due largely to metabolic causes, one would expect that both kidneys would be equally subjected to the same metabolic factors and that there would then be a much

higher percentage of bilateral stones. The fact that this is not the case seems to indicate that local factors are of great importance.

MODERATOR MARSHALL: *Can you mention two or three of these local factors which you have in mind?*

DR. TWINEM: There may be local factors in the form of poor drainage of a kidney, which may be the result of stricture at the ureteropelvic junction, infundibular narrowing, unusual calyceal dependencies, marked angulation of a calyx, or infection of the whole kidney or of one calyx only.

MODERATOR MARSHALL: *Do you accept Randall's plaques as an explanation?*

DR. TWINEM: I don't profess to know much about Randall's plaques. They appear to be a reasonable explanation for some calculi. I do not believe they can account for all of them.

MODERATOR MARSHALL: Randall's observations were most interesting, but thus far that remark describes them nearly completely. People pay lip service to his work, but there does not seem to be much confirmation, so far, and certainly little of a practical clinical nature has developed from that study as yet. Recently, in the *British Journal of Urology;* there was a report of a somewhat related account of causation having to do with the formation of microliths in the renal lymphatic system.

Dr. Spellman, what do you think is the most interesting current theory about the formation of ordinary kidney stones?

DR. SPELLMAN: Apparently the etiology of kidney stone formation will become clearer as further facts concerning the physiology of collagen material and epithelium are revealed. There appear to be three materials in the kidney that contribute to stone formation: the connective tissue; the lining tissue or mucosa; and the serum containing the calcium and phosphate ions. These materials combine in some way to produce a stone which is, as we know, composed of mineral crystals held together by a matrix.

MODERATOR MARSHALL: I have heard this matrix spoken of as "uromucoid".

DR. SPELLMAN: The matrix of a stone is much like the matrix of bone or osteoid tissue. Since an actual progressive stone is not produced by the simple salting out of calcium and phosphate crystals in a supersaturated solution, something else is required to hold these crystals

together. This other material seems to be a sticky, sugar-protein combination, and apparently it can be found free in the urine. On this account, Boyce has called it uromucoid. Recent investigations seem to show that the level of this material in the urine is elevated three to 13 times in patients with hyperparathyroidism or renal infection, in those on cortisone or ACTH medication, in patients with repeated stone formation, and in experimental animals subjected to repeated stress. There seem to be several varieties of this mucoprotein in the urine. Boyce thinks that the physical properties are related to the state of polymerization. With depolymerization into smaller molecules the affinity for calcium is thought by Boyce to increase greatly.

MODERATOR MARSHALL: *All this is a new idea?*

DR. SPELLMAN: It certainly is.

MODERATOR MARSHALL: *Where does this mucoprotein come from? Is it merely filtered through the kidney?*

DR. SPELLMAN: This mucoprotein molecule is apparently of tremendous size, and I would think it unlikely that it would go through a normal glomerulus.

MODERATOR MARSHALL: *How do you think it might get into the urine?*

DR. SPELLMAN: A major disease of the nephron might permit it to pass, but there is no evidence that such disorder regularly precedes calculous formation. The material can be broken into much smaller molecules and I presume that this might occur across the urinary mucosa. After studying this problem Dr. Roger Baker believes that calculous formation has three important steps: first, an increase in the amount of ground substance (possibly mucoprotein) under the tubular epithelium; second, calcification of this material; and third, a similar process taking place simultaneously in the lumen of the tubule.

MODERATOR MARSHALL: There is a lot of interest in this matter, but we cannot go on with it now, especially as we don't know enough. We have transplanted transitional epithelium as a free graft in experimental animals to investigate further the physiology of the mucosa. This transplanted mucosa does elaborate a fluid which apparently stimulates true osteogenesis in certain connective tissues of the dog. We also have some incomplete evidence that the fluid elaborated by the mucosa contains material very similar to the mucoprotein studied by Boyce. Clinical application of this information is, however, not yet apparent.

DR. TWINEM: I would like to ask Dr. Spellman why these disease processes, or at least abnormal occurrences, should not affect both kidneys equally.

DR. SPELLMAN: That is a good question, which I cannot answer, except to say that the opposite kidney forms a calculus much more frequently in a patient who has had a stone than in those others in the general population.

MODERATOR MARSHALL: *Dr. Oppenheimer has looked up recurrence rates. What are the recurrence rates of renal calculi?*

DR. OPPENHEIMER: In general the recurrence rate seems to vary from 4 per cent to 60 per cent.

MODERATOR MARSHALL: *What is the recurrence rate for different kinds of stones?*

DR. OPPENHEIMER: Before I give any statistics, an explanation of terminology is indicated. I am not sure, for instance, that when I say that stones are bilateral in 25 per cent of cases it means the same thing as when Dr. Twinem says they are bilateral.

MODERATOR MARSHALL: *What do you mean then when you say 25 per cent?*

DR. OPPENHEIMER: In my statistics, which were reported in *Surgery, Gynecology and Obstetrics*, December 1937, I explained that bilaterality meant the appearance of calculi on both sides at any time during the life, and/or while the patient is under observation. I am sure that the incidence of bilaterality is less than 25 per cent because this figure refers only to in-hospital patients.

Also, when we talk about recurrences, we must differentiate between true recurrences and pseudo or residual recurrences. The total recurrence rate is the sum of the true recurrence rate plus the residual or pseudo-recurrence rate. The residual recurrence rate is the rate of recurrence in a kidney where radiography shows that stones have been left behind after operation. This is determined by x-raying the patient shortly after the operation.

MODERATOR MARSHALL: *What were these rates?*

DR. OPPENHEIMER: The true recurrence rates in all types of cases for pyelolithotomy, pyelonephrolithotomy and nephrolithotomy were respectively 14.9 per cent, 32.0 per cent and 29.4 per cent. The total rates of the true recurrences plus the residual recurrences were 24.0 per cent, 54.0 per cent and 58.6 per cent respectively. In unilateral cases

the true recurrence rate for all conservative operations in the primary stone cases (calcium oxalate or calcium oxalate-calcium phosphate) was 8.1 per cent; while in the secondary stone cases (mixed calculi, salts of the alkaline earths) it was 28.3 per cent.

MODERATOR MARSHALL: *The recurrence rate of uric acid calculi was not stated. Many of them are tiny things and are rarely seen in our offices. Also, we frequently fail to get an accurate follow-up in such cases. Dr. Oppenheimer, do you have another reason in mind?*

DR. OPPENHEIMER: Another reason is that one often cannot tell radiographically when there *is* a recurrence of the uric acid stone.

MODERATOR MARSHALL: *What is the recurrence rate of staghorn phosphatic calculi?*

DR. OPPENHEIMER: The true recurrence rate of phosphatic or dendritic stones was 30 per cent, but the total recurrence rate was about 60 per cent.

MODERATOR MARSHALL: *That 60 per cent includes the false recurrences, the little pieces left behind that later grew?*

DR. OPPENHEIMER: Sometimes large pieces are left behind.

MODERATOR MARSHALL: *Accordingly, a great deal depends on whether the removal of the staghorn has been really complete?*

DR. OPPENHEIMER: That's right.

MODERATOR MARSHALL: *Dr. Twinem, do your studies indicate essentially the same figures as those given by Dr. Oppenheimer, and are the figures of the Lincoln Hospital about the same?*

DR. TWINEM: Yes. In the series that I studied, recurrence of staghorn calculi was about 40 per cent when checked by x-rays a few years postoperatively.

MODERATOR MARSHALL: *Dr. Oppenheimer, what measures do you use to insure the complete removal? That is, do you always take x-rays in the operating room?*

DR. OPPENHEIMER: I wish I knew how to prevent residual calculi, because I believe we would get better results and have fewer recurrences if we could accomplish complete removal of all stones.

MODERATOR MARSHALL: *Would you tell us your little tricks?*

DR. OPPENHEIMER: I think the most important measures are to operate slowly and to palpate carefully when finished, to explore the calyces with stone forceps and scoops, and to irrigate with a catheter. I have often seen small stones washed out of the kidney pelvis with irrigation.

Operative x-ray control can help locate the stone fragments which are not palpable. I think operative x-ray control should be used much more often than it is at present.

MODERATOR MARSHALL: *How often do you use it?*

DR. OPPENHEIMER: We try to use operative x-ray control for all complicated or dendritic stones.

MODERATOR MARSHALL: It is a cumbersome procedure and it is sometimes difficult to line up the personnel.

DR. OPPENHEIMER: It is cumbersome. Recently, I had some false hopes about a portable source of radiant energy, a little lead box with a shutter which we tried to use as a source of radiation. Our roentgenologist said it wasn't very practical, but it would be a very nice thing if one could have a little box instead of the bulky portable x-ray machine.

MODERATOR MARSHALL: *Something like a flashlight?*

DR. OPPENHEIMER: Yes,—to put in front of the kidney, open the shutter, get your picture, and have it back in a few minutes.

MODERATOR MARSHALL: *Have you used Dees' coagulation pyelolithotomy?*

DR. SPELLMAN: I have used it twice. The first time it didn't work well, most likely because of my inability to follow the instructions properly. The second time it worked well. It surprised me. It formed a nice, heavy clot, which on extraction contained numerous small stones within it.

MODERATOR MARSHALL: We have used it about a dozen times altogether. At least three or four failures have been the result of what Dr. Spellman has described as technical difficulties. Since one doesn't use it often, the possibility of getting the procedure confused, and hence a poor result, has been significant. Three or four of the 12 were really beautiful operations. If there is a small, narrow opening into one calyx, the stone may be too large to come through even if it is solidly within the coagulum. Actually, I think the method should be studied more carefully and used by a variety of urologists.

DR. OPPENHEIMER: Isn't it true that you sometimes accidentally use the same method when there is bleeding?

MODERATOR MARSHALL: Yes.

DR. OPPENHEIMER: With good results?

MODERATOR MARSHALL: Yes, we do have clots in our kidneys—

rather too often, I might say.

Dr. Slaughter, you are the authority on technique for removing these staghorns. How does one go about it?

DR. SLAUGHTER: I think the movie will best demonstrate the technique.

(At this point a color motion picture was shown of the removal of staghorn calculi.)

In bisecting the kidney we really mean bisecting it. I think you will see this as the picture progresses. In the past 14 years I have not removed a single kidney for stones. In the movie here you see how much pressure lies back of the stone within the kidney. Although it does not show here in the film, we have put on a Doyen clamp at the pedicle. I find this the most satisfactory instrument for that purpose. I have never once removed the clamp during the procedure. I believe that it is entirely unnecessary to take off the clamp. If you do, you lose five or six minutes while the blood is draining from the kidney. Recent work shows that no damage will result to kidney function within two hours after applying the clamp to the pedicle. One hour and 18 minutes is the longest time I have left the clamp in place. In that time we have removed 2,500 small stones from a kidney; and I am glad to say we got them all. I have, however, left stones behind. I do not hesitate to go back immediately if a patient is found to have stones remaining—certainly before the patient leaves the hospital. It is my opinion that if we do not remove all the stones the operation is a failure and should not have been attempted in the first place.

MODERATOR MARSHALL: *How avascular is Broedel's line?*

DR. SLAUGHTER: There is such a line. On four occasions in the last 150 attempts we have hit Broedel's line, and it wasn't the last four cases either. It is rather spectacular when you hit it, and if you do, there is absolutely no bleeding when the clamp is removed. It is fantastic, but it's true.

MODERATOR MARSHALL: *How did you pick the line in those four cases?*

DR. SLAUGHTER: The same way I picked all the other 146!

MODERATOR MARSHALL: That is a 2.6 per cent success rate.

DR. SLAUGHTER: About that.

(Concurrent comment during showing of film.) The kidney is exposed in routine fashion. It doesn't make too much difference how you

expose it, but it is important to preserve the capsule at all cost.

The kidney at this point is bisected along Broedel's line. There have been many methods suggested for the opening of the kidney. You will notice that we open it sharply from end to end, and it is really open. It is not a "medical incision"! I never close the kidney without going back four times and exploring each calyx with my finger. I find that the most satisfactory way to find all the stones. One can usually feel them. Here we are actually opening a calyx by sharp dissection. The calculus is exposed. This next stone was down pretty close to the pelvis. Here it comes out. It looks not unlike a lobster. You might also note that a gallbladder spoon was used. A gallbladder spoon is really an excellent instrument for getting all small stones out of the calyces. Here are the stones. These little arteries should be identified and closed with small mattress sutures. You need not worry about the veins but you do need to worry about the arteries because they will really give trouble.

MODERATOR MARSHALL: *In cases of split kidneys, how many times have you had to go back and remove the kidney in the early post-operative course?*

DR. SLAUGHTER: I have never gone back and had to remove the kidney. I did go back on one occasion because the sutures used gave way. This was ten years ago. I went back and repaired the kidney again and the patient made an uneventful recovery.

MODERATOR MARSHALL: *We have split 18 kidneys and have had to take out three for hemorrhage. We probably could have gotten by with one. Why do you think we have had such hemorrhages?*

DR. SLAUGHTER: I don't know. I wonder if you used all three stages of this operation. The capsular suture should be placed first. If it is not, you will never be able to place it properly.

MODERATOR MARSHALL: It is true that we haven't usually used a capsular stitch.

DR. SLAUGHTER: During experimental days I did leave out the capsular suture to see what would happen. About eight days postoperatively we had a fair amount of bleeding. I believe that the hemostatic suture, which you will see in a moment, gave way. The capsule was not there and the kidney then opened up. I think one should use the capsular suture and use ribbon gut instead of ordinary catgut. Ribbon gut effects more solid compression rather than localized compression.

With the capsular suture in place, we are now ready to put in the hemostatic sutures. They consist of a piece of ribbon gut on either side around which the mattress sutures are pulled tightly so that it gives compression not only at the point of suture but also gives compression between these points. Now the ribbon gut is being placed. I have operated in hospitals where they did not have ribbon gut and have taken six or eight plain strands of catgut and used that in place of ribbon gut.

MODERATOR MARSHALL: *I have left a nephrostomy tube in place after a split, usually for two weeks. Doesn't your suture go through the ribbon gut?*

DR. SLAUGHTER: It does not go through the ribbon gut. Formerly I used to put it through the ribbon gut, but that is difficult and actually serves no useful purpose.

You will find that you will have urine draining from the nephrostomy tube long before the wound is closed.

I think you should use all the steps. The vessels within the kidney must be sewn; you must approximate the capsule; and you must use the ribbon gut, or its equivalent, so that you have continuous pressure.

MODERATOR MARSHALL: *Dr. Slaughter, how many times have you left stones behind, that you could detect by x-ray, after this technique?*

DR. SLAUGHTER: Very few, actually, but it is a long hard process to make sure they are all out.

MODERATOR MARSHALL: *Dr. Spellman, how many stones did we leave in the 18 splits that we did?*

DR. SPELLMAN: We left two.

MODERATOR MARSHALL: Two pieces of stone in 18 cases, that seems fairly good.

DR. SLAUGHTER: May I ask, did you go back and take them out?

DR. SPELLMAN: No, we didn't. The patients had had enough—and we too!

MODERATOR MARSHALL: We did not use the capsular stitch regularly. We did try to follow every other step. I must say, however, that although I was not greatly impressed with the capsular stitch it now appears that we should "put up or shut up" since Dr. Slaughter's program has worked out significantly better than ours.

Dr. Slaughter, would you be deterred from splitting a solitary kidney?

DR. SLAUGHTER: No, I have split a solitary kidney on nine occasions.

One of these cases is of interest: A patient called me from Paris one morning at 4 o'clock and said he had a solitary kidney and had been in anuria for 36 hours. I told him to get on an airplane and come over, and that's what he did. I split the kidney, put in a nephrostomy tube, allowed a lower ureteral stone to pass, and the patient made an uneventful recovery.

DR. OPPENHEIMER: Did Dr. Slaughter say he split the same solitary kidney nine times?

DR. SLAUGHTER: No, I have split nine solitary kidneys.

MODERATOR MARSHALL: *Which kidneys would you not split?*

DR. SLAUGHTER: I have never seen a kidney I would not split.

MODERATOR MARSHALL: *Have you seen a kidney that you would not split, Dr. Twinem?*

DR. TWINEM: Oh, yes.

MODERATOR MARSHALL: *Quite a few?*

DR. TWINEM: I don't look with quite the same degree of complacency on splitting a kidney as George Slaughter does. Yes, I think if you have a dendritic calculus and the patient is 65 years old and that calculus is causing no trouble, the function of the kidney is good, no infection is present—

MODERATOR MARSHALL: *How often do you see a staghorn with no infection?*

DR. TWINEM: You see that in about 15 per cent or 20 per cent of cases. In the case just described I would let the staghorn calculus remain. But there are some I would not split because I would perform a nephrectomy.

MODERATOR MARSHALL: *How about splitting the solitary kidney? Dr. Slaughter said he split them with no hesitation.*

DR. TWINEM: I would split it under certain circumstances.

MODERATOR MARSHALL: *Not as readily as Dr. Slaughter, I gather. Would you split it as readily as Dr. Slaughter, Dr. Oppenheimer?*

DR. OPPENHEIMER: About half as readily.

MODERATOR MARSHALL: *How about you, Dr. Spellman?*

DR. SPELLMAN: About two-thirds as readily.

MODERATOR MARSHALL: I would not split kidneys quite as readily as Dr. Slaughter and certainly not as readily if that were the patient's only kidney.

DR. SLAUGHTER: I am frank in confessing that I would not split a

solitary kidney unless and until I was absolutely sure of my method. I had done about 40 splits before I did the first solitary kidney. Perhaps I am a little over-confident, but the nine have worked out extremely well.

MODERATOR MARSHALL: *Have any of your patients developed hypertension postoperatively?*

DR. SLAUGHTER: None.

MODERATOR MARSHALL: *What is the recurrence rate following extensive nephrolithotomy with the usual prophylactic measures such as antiseptic drugs and increased fluids?*

DR. SPELLMAN: Dr. Edward Brady, of Bellevue Hospital reviewed 19 extensive nephrolithotomies for dendritic calculi. It is safe to say they weren't put on any major prophylatic treatment. He found an 80 per cent recurrence rate, which is a little higher than the percentage that has been stated tonight.

DR. TWINEM: May I add something here? I wouldn't split some kidneys for the reason that I would remove them. If you have a kidney with a staghorn calculus associated with infection and the other kidney is free of stone, and has always been a good functioning kidney, never infected, never the site of stone formation, I believe that the best you can do then is to remove the kidney with the dendritic calculus. As to recurrence, I will take a bet with anybody that if you take any series of splits for staghorn calculi and follow the series for four years and check the patients with x-ray, that you will find a recurrence rate of 25 per cent as a minimum.

MODERATOR MARSHALL: *What do you think the recurrence rate would be in two years? I ask that, because we have some figures.*

DR. TWINEM: In two years it would be definitely less. There is quite a difference. Sutherland, in England, studied 89 cases of stone recurrence in which only 25, or 28 per cent recurred in the first two years. The others recurred later than two years. Fifty-eight per cent of the recurrences were within five years.

MODERATOR MARSHALL: *What is the recurrence rate in the opposite kidney after a split, two years later, or perhaps in four years?*

DR. TWINEM: The recurrence rate in the opposite kidney was 4 per cent following operations for dendritic calculi.

MODERATOR MARSHALL: *In the opposite kidney?*

DR. TWINEM: Yes.

MODERATOR MARSHALL: *Dr. Oppenheimer, have you seen spontaneous dissolution of calculi?*

DR. OPPENHEIMER: I have, but before I present that matter I have a case I would like to tell you about. I think we should stress the point that our recurrence rates depend upon the length of follow-up. I would also like to point out to the audience that the article by Dr. Sutherland, in the *British Journal of Urology* for March, 1954, mentioned by Dr. Twinem, reports probably the best set of recurrence statistics that I have seen since Dr. Twinem and I wrote similar articles. Do you agree?

DR. TWINEM: Since you wrote yours!

DR. OPPENHEIMER: We have all tried to dissolve stones, using especially Suby's solution, generally with equivocal success. In our hands the acid ash diet with Vitamin A has been unsuccessful, although I know Dr. Higgins has reported some successes.

The patient whom I wish to tell you about was a 49-year old Turkish Jewess who first came under observation on our ward service about 1949 with a 10 year history of bilateral dendritic calculi. She was also a mild diabetic. Both kidneys were infected and showed some diminution of function. Salmonella Montevideo was cultured from the urine. Other investigations gave essentially negative results. She had a right nephrolithotomy with residual calculi, in spite of operative x-ray control. Later a perinephric abscess formed, was drained, and was followed by a temporary right renal fistula. The films showed a gradual spontaneous disappearance of the untreated left dendritic calculus until only a dense nucleus 3 x 2 cm. and one smaller concretion remained. This occurred over a period of one and a half years. Recently I read an article on experimental urolithiasis in which stones did not form on a vesical foreign body infected with an unusual Salmonella. Whether the diabetes and infection are related to the dissolution of the stone can only be conjectured. I referred the patient to Dr. Shorr so that he might investigate her from the metabolic point of view.

MODERATOR MARSHALL: *Does an acid ash diet, in your opinion, prevent phosphatic stones?*

DR. OPPENHEIMER: I don't know, but I doubt it.

MODERATOR MARSHALL: *Dr. Spellman, how does hyaluronidase control recurrence?*

DR. SPELLMAN: My brief experiences with hyaluronidase have been failures.

MODERATOR MARSHALL: *What place has partial nephrectomy in prophylaxis and prevention of recurrence?*

DR. TWINEM: I think it is a very valuable procedure when stones have formed in the tip of a calyx which has poor drainage by reason of a strictured infundibular portion or by reason of dependency and angulation with the pelvis—where a dysuric type of calyx is present. I began doing partial nephrectomies in 1937, and have found that one rarely gets a recurrence if the kidney is of the type in which there is one such calyx while the others drain well. The largest series I know of was reported by Dr. H. H. Stewart of Bradford, England. He reported 87 cases of partial nephrectomy checked two to 13 years postoperatively with x-rays. He found a recurrence rate of 6.8 per cent, which I think is quite good for a large series.

MODERATOR MARSHALL: *In other words, you think for selected cases it is highly desirable?*

DR. TWINEM: Yes.

MODERATOR MARSHALL: We will now touch on the Shorr regimen, not only because we are much interested, but also because Dr. Shorr is here in the audience.

Dr. Spellman, in your experience, how effective is the Shorr regimen? How does a 1300 milligram phosphatic intake in 24 hours with 40 cc. of aluminum carbonate gel (Basaljel) work out? I should also add,—with examination of the 24-hour urines to make sure that you are getting the desired effect. How effective has that program been in reducing recurrences following a split for staghorns of the type that Dr. Slaughter has shown? We have said that somewhere between 25 per cent and 80 per cent will recur in a period of approximately two years probably nearer the higher figure.

DR. SPELLMAN: From our experience, the program is very worth while. We have reviewed 18 consecutive extensive nephrolithotomies from the New York Hospital. Eleven of these patients were faithful to the regimen and were followed for an average of three and one-half years. Not one of the 11 had a recurrence in that period. Three nephrectomies were necessary, as already mentioned by Dr. Marshall. Two patients were complex, one with hyperparathyroidism, and so will be omitted for brevity now. One of the remaining patients was sent home and inadvertently not placed on the Shorr regimen. Within three months she developed a recurrence and was then placed on the regimen.

The stone failed to grow during the next two years. The stone was then surgically removed and there has been no recurrence while the patient has been on the program in the subsequent three years of follow-up. A more important case, however, was that of an alcoholic with bilateral staghorn calculi. He had complete bilateral nephrolithotomies. The patient did not follow the Shorr program originally and had recurrences. When the program was subsequently followed, the stones stopped growing. Later he stopped the program and the stones began to grow again. While reviewing the literature I discovered a similar case discussed by Dr. Elmer Hess.

MODERATOR MARSHALL: We are fortunate to have Dr. Shorr's laboratory to aid us in following these patients. It is not a perfect program, for a number of reasons, and I am sure that once in a while there will be a patient who doesn't respond. Dr. Twinem has had one such individual, whose phosphatic stones grew in spite of the patient being on the program, but that is exceedingly rare. We have a number of cases in which patients would be on the regimen for significant periods and form no stones; then they would go off it and stones would come back. *If it is so good, Dr. Spellman, why isn't it more popular?*

DR. SPELLMAN: I don't think urologists in general are convinced that it is such a good program; therefore they fail to "sell" the program to the patient. After all, there have been many programs proposed which eventually have not turned out to be effective. The patient must be sold on the idea. The diet isn't too easy to stay on. The program is constipating and, in general, is annoying. If one really wants to follow these patients carefully, one should check their urinary output of calcium and phosphorus rather frequently. Dr. Marshall had a patient who continued to form stones despite the program and normal urine values. After some detective work, he discovered that she followed the program only while she was collecting the urine specimens.

MODERATOR MARSHALL: We had one instance in which we couldn't determine why the patient continued to develop stones in spite of being on the Shorr program. The first night he was readmitted for study he asked for his milk and cream, because he was following not only the Shorr regimen but also a Sippy program for peptic ulcer. You do have to get the enthusiastic cooperation of the patient. The constipation factor can be controlled by ordinary medical means, but it can be most annoying.

The thing about the Shorr program that particularly appeals to me, is that it works in the patient who needs it most. It works in the face of alkalinizing infection. If the patient has a lot of Proteus infection you can acidify in the area around the glomerulus, but the acidity won't be adequate in the region where the stone is actually growing. In addition, in many patients low renal function will not permit the degree of acidosis obtained with an acidification program. This is not a drawback to the Shorr regimen. In fact, there might be less burden on the kidney. Accordingly, the Shorr regimen is ideal for the old chronic stone-former of phosphatic calculi who has had one stone after another with infection and disabled kidneys. It is this type of patient that the Shorr regimen works on,—indeed, works on the best. He is the patient who is scared to death and who will stay on the diet and take his gel—and bring accurate urines for checking. The diet is not bad, it is just monotonous. Also, the Basaljel is dull. One must have laboratory control, too, for the Shorr regimen. If you don't have this control you can't pick up the simple deviations from true failures. Measuring the 24-hour creatinine is important, as it is a check-up on the collection of the specimens—since the total output in 24 hours under usual conditions is about the same.

Dr. Slaughter, if a patient has stones on both sides, with one side not as good as the other, would you operate first on the good side or the bad side?

DR. SLAUGHTER: I would operate on the bad side first; I always have.

MODERATOR MARSHALL: Why?

DR. SLAUGHTER: Because you then have the better kidney to carry you through the first operation; then after the first operation you have a good kidney on the opposite side when you attack the originally better kidney.

MODERATOR MARSHALL: *In general, does the rest of the panel agree with that statement?*

DR. OPPENHEIMER: In general, I think that is true. On the other hand, I think you should individualize each particular case and not follow a rule.

MODERATOR MARSHALL: Dr. Slaughter does have a rule, however.

DR. SLAUGHTER: I have a rule.

MODERATOR MARSHALL: *Do you agree with the rule as laid down by Dr. Slaughter, Dr. Twinem?*

DR. TWINEM: I think there should be no set rule, because in general

one should operate on the better kidney first. If the better kidney has a small stone in it which may cause blockage, then I would operate on the better kidney first so that blockage would not occur postoperatively. Also, in some cases there may be a question as to whether the poorer kidney should be *removed* or not. If you operate on the better kidney first and get it into good condition, then you can readily operate on the worse kidney. You can examine it carefully and then, with more or less equanimity, decide whether the kidney should be removed or not. If you operate upon the poorer kidney first you will be less able to decide this point. I agree with Dr. Oppenheimer: each case should be individualized.

MODERATOR MARSHALL: *Here is a question from the audience: Where does urinary surface tension fit into the picture of recurrent urinary calculi?*

DR. SPELLMAN: Much of this urinary surface tension problem is beyond me. We do know that the large muco-protein molecule increases the surface tension; the smaller molecules lower it (such as the glucuronides). What this actually has to do with renal calculous formation remains to be explained. I think the answer lies in our better understanding of the collagen system and also the physiology of the mucosa itself.

MODERATOR MARSHALL: The whole subject of these colloids in the urine is relatively new and not well understood. Surface tension is probably related in some way, as yet undetermined. Dr. Harlin of Brooklyn has worked on this problem and has obtained some interesting findings, but they are all rather new and have not been evaluated.

Here is another question from the audience: Would you carry a woman through pregnancy on the Shorr regimen? I can answer that one: We have done so on several occasions and nothing untoward has happened, either to the mother or the child.

Dr. Slaughter, what do you do with a small renal infarct noted during a renal split?

DR. SLAUGHTER: I have never encountered it, but I would remove it.

MODERATOR MARSHALL: I have seen one noticeable infarct during a kidney split operation. The postoperative hemorrhage did come from that infarcted area.

Another question from the audience: How long should a patient be kept on a diet to prevent recurrence of calculi? By the use of the word

"diet" I presume the Shorr regimen is meant.

DR. SPELLMAN: I like the statement that Dr. Hess has made—that once a patient has a staghorn stone he is a urological problem for life. One certainly has to individualize cases. I think it is advisable, even after a simple nephrolithotomy, to use the program for at least six to nine months, to prevent a recurrence in the operative area. Chronic stone formers should probably follow the program indefinitely.

MODERATOR MARSHALL: Nobody knows just how long, but it had better be longer than shorter.

DR. OPPENHEIMER: Dr. Marshall, in some stone statistics 10 per cent of the total number of stones recurring, did so after 15 years.

MODERATOR MARSHALL: If you tell the patients to continue on the regimen indefinitely, you have advised them correctly although this advice as to time may possibly exceed the necessary requirement.

Here is a question about the use of the Shorr regimen in growing children. We have had so few children with phosphatic stones on the regimen that I cannot answer the question except to say that we have put young patients (five years of age) on it, and have kept them on it for many months without significant troubles. What may happen to these patients in 15 or 20 years I can't say, because we have insufficient experience. We have had patients who developed a little osteoporosis, but that's about all. After all, this is not a diet in which there is no phosphorus. The phosphorus is just moderately low.

Another question: Of what value is the determination of urinary creatinine in the stone former?

DR. TWINEM: I think the value would be little, except in cases where stone formation is very advanced and kidney function is poor.

MODERATOR MARSHALL: It might show that the patient had poor renal function.

DR. SLAUGHTER: I agree.

DR. SPELLMAN: It is a fairly constant item in the urine, thereby enabling one to tell if a full 24-hour specimen has been submitted for analysis of the calcium and phosphorus levels.

MODERATOR MARSHALL: *It appears to me like a metabolic problem. Is not the relation between creatinine and muscle partly a phosphatic problem?*

DR. EPHRAIM SHORR (from the audience): It is, if there is coincidental disease with impairment of the muscle metabolism. If the patient loses

weight, then it will fall. It was suggested some years ago that estrogens might be useful as they would increase the output of citrate and at the same time decrease the calcium output in the urine.

DR. SPELLMAN: We haven't had a clinical program to test the estrogen idea, but it does sound reasonable.

DR. TWINEM: I tried to use estrogens but most of the patients didn't like the effects.

MODERATOR MARSHALL: Women who have a uterus may well have difficulties on an estrogen program. If the urine is infected, the organisms apparently use up the citrate and it doesn't have much effect. Men usually don't like the effect of estrogens, for obvious reasons.

Another question from the floor: Has any work been done with heparin in dissolving kidney stones? Has anyone on the panel had any experience with heparin for this purpose?

PANEL: No experience.

DR. OPPENHEIMER: Has anyone on the panel had any success with Versene?

MODERATOR MARSHALL: We have used Versene several times without beneficial results. It is definitely irritating. We have had a few minor successes in dissolving soft stones, really mud, with G-solution; but we have had a minimum of success with the hard, well-formed calculus.

Dr. Twinem, will a change in climate, physical activity, or geographical location reduce the recurrences of the stone-former? In other words, is it a good idea for him to go to Florida or to some other escapist place?

DR. TWINEM: I don't believe climate will have any effect in such a case. If a person has a tendency to form stones and he goes to a very warm climate, his urine will be more concentrated. He may lose more moisture by perspiration. During the war in the Pacific area, a great many young men formed small stones in a higher proportion than they do at home, probably because of their very concentrated urine.

MODERATOR MARSHALL: Vitamin-A deficiency, Randall's plaques, small infarcts, recurrent infections, areas of fibrosis, dehydration, arteriosclerosis, stress and strain, have all been proposed at one time or another as significant causes of calculi. If these conditions play a significant role, it would seem that the incidence of stones should increase with age,—the longer one lives, the more likely would be the probability of these conditions arising and causing stone formation. Renal stones

ought to be a major cause of death in old age, but actually the incidence of first renal stones is not great at all in the later years of life. We have had one child of two years who formed idiopathic renal stones and I have seen only one person who, on clear evidence, formed the first renal phosphatic stone after the age of 65. The vast majority of first renal stones occur between 20 and 55 years of age. *Can you explain this incidence rate?*

DR. SLAUGHTER: No, that's why I have to split kidneys.

DR. TWINEM: Bladder stones do increase definitely with age. Kidney stones are more frequent in middle age.

MODERATOR MARSHALL: We are talking about kidney stones. The reason that urinary stones increase with age in men is obvious, because of the prostatic obstruction. You may have infection associated with the obstruction. I think that this shows the importance of these factors, whether it be applied to bladder or kidney. *Do you have a clear idea, Dr. Slaughter?*

DR. SLAUGHTER: I do not.

DR. OPPENHEIMER: I know nothing about stones after tonight!

MODERATOR MARSHALL: *Dr. Spellman?*

DR. SPELLMAN: No.

MODERATOR MARSHALL: I think we might end on that note, showing that there are many things we don't know about stones.

Question from the floor: *Dr. Slaughter, how many times have you done a second or third bisection on a solitary kidney?*

DR. SLAUGHTER: Never on a solitary kidney.

Question from the floor: *I would like to ask Dr. Slaughter what he does about associated lesions in the upper urinary tract in cases where he split the kidney.*

DR. SLAUGHTER: If there is any major disorder in the upper urinary tract, we repair that. We always do that at the same time.

Question from the floor: How about oxycel?

DR. SLAUGHTER: I don't like it. It is a foreign body, can cause difficulties and is unnecessary.

DR. JAMES J. TOOMEY: Unless there is an urgent question we must bring this meeting to a close. On behalf of the Section on Genito-Urinary Surgery of the Academy, I wish to thank our panel members for their interesting and stimulating discussion.

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Freud and Psychiatry ..... Kenneth E. Appel
Freud and Medicine ..... Roy R. Grinker
Freud and Prophylaxis ..... Paul V. Lemkau

Dinner – Subscription ($10.00) – 6:30 to 8:00 P.M.

Evening Session – 8:30 P.M.

Presiding Chairman ..... Iago Galdston

Freud in the Perspective of Medical History ..... Gregory Zilboorg
The Impact of Freud Upon Anthropology ..... Clyde Kluckhohn
Freud's Influence in Contemporary Culture ..... Speaker to be announced

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2. The Fund will be expended only in grants-in-aid for investigation or scholarships for research in bacteriology or sanitary science. Expenditures may be made for: (a) Securing of technical help. (b) Aid in publishing original work. (c) Purchase of necessary books or apparatus.

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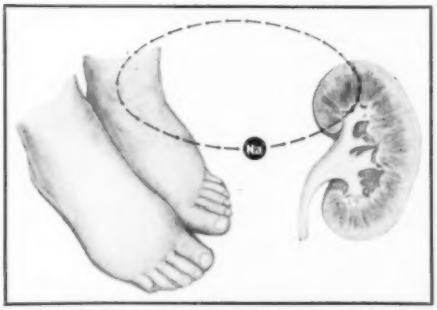

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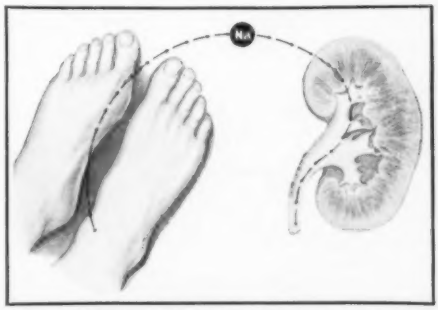

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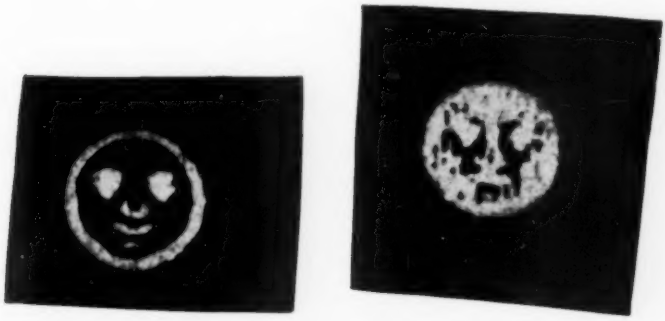

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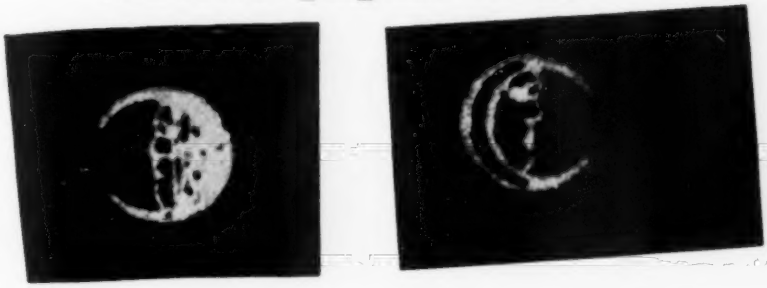

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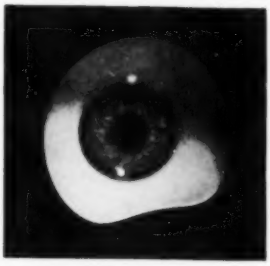

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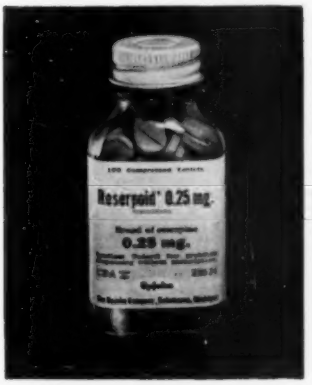

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1. J.A.M.A. 159:645 (Oct. 15) 1955.
2. J.A.M.A. 158:386 (June 4) 1955.

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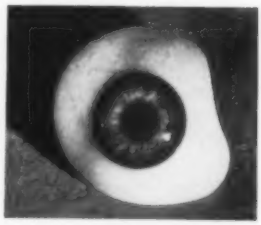

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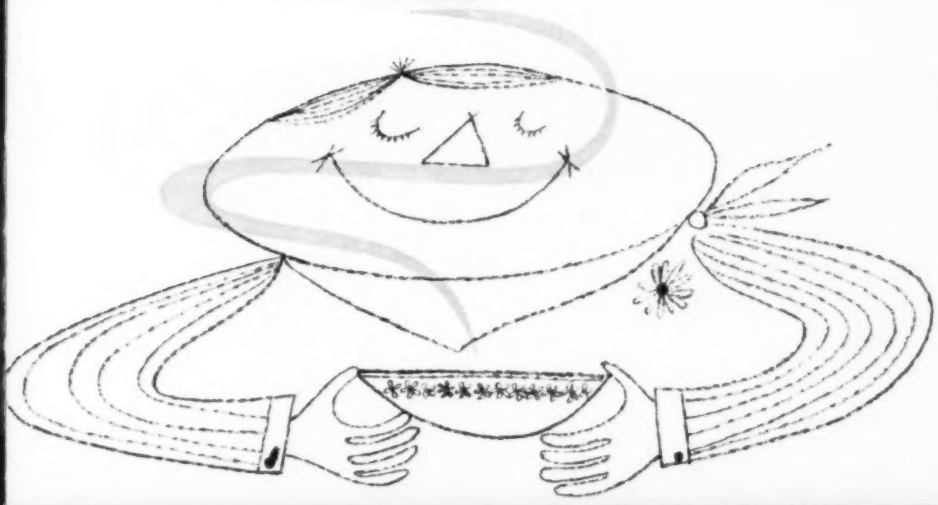


salt-free needn't mean flavor-free

DIASAL is enthusiastically endorsed by low-salt dieters for the zest and flavor it gives to pallid, sodium-restricted meals. So closely does it match the appearance, texture and taste of table salt that patient adherence to your diet instructions is virtually assured.

DIASAL contains only potassium chloride, glutamic acid and inert ingredients...no sodium, lithium, or ammonium. It may be used safely for extended periods, both at the table and in cooking. Because of its potassium, DIASAL may be a valuable prophylactic against potassium depletion.

DIASAL®

packaging: available in 2-ounce shakers and 8-ounce bottles.
Send for liberal supplies of tasting samples and low-sodium diet sheets for your patients.

FOUGERA

E. FOUGERA & COMPANY, INC.
75 Varick Street, New York 13, N. Y.

ISOLATE
THE
ULCER!
Since the ulcer patient usually can not get away from it all, prescribe MONODRAL with MEBARAL to more effectively isolate the ulcer from the patient physiologically.
MONODRAL with MEBARAL controls hyperacidity by a proved superior antisecretory action.
Controls hyperirritability and hypermotility of the upper gastro-intestinal tract, relieves pylorospasm.
Induces a serenity of mind without affecting mental alertness, softens the emotional impact of environmental stimuli.
Controls the psychovisceral component of peptic ulcer; lessens gastro-intestinal tension by diminishing reflex motor irritability.
MONODRAL with MEBARAL Tablets, 1 or 2 tablets three or four times daily; each tablet containing 5 mg. MONODRAL bromide and 32 mg. MEBARAL. Bottles of 100 tablets.
Winthrop
LABORATORIES
New York
Windsor, Ont.
MONODRAL® with MEBARAL®
FOR COMPLETE CONTROL
of peptic ulcer
Monodral (brand of penthienate) and Mebaral (brand of mephobarbital), trademarks reg. U.S. Pat. Off.

Lift the depressed patient up to normal without fear of overstimulation . . .

with new

Ritalin®

A HAPPY MEDIUM IN PSYCHOMOTOR STIMULATION

• *Boosts the spirits, relieves physical fatigue and mental depression . . . yet has no appreciable effect on blood pressure, pulse rate or appetite.*

Ritalin is a mild, safer central-nervous-system stimulant which gently improves mood, relieves psychogenic fatigue "without let-down or jitters . . ."[1] and counteracts oversedation caused by barbiturates, chlorpromazine, rauwolfia, and antihistamines.

Ritalin is "a more effective and less over-reactive drug than amphetamine or its derivatives."[2] It does not produce the "palpitation, nervousness, jitteriness, or undue pressure in the chest area . . . so frequently mentioned by patients on [dextro-amphetamine sulfate]."[3]

Dosage: 5 to 20 mg. b.i.d. or t.i.d., adjusted to the individual.

RITALIN® hydrochloride (methyl-phenidylacetate hydrochloride CIBA)

References: 1. Pocock, D. G.: Personal communication. 2. Harding, C. W.: Personal communication. 3. Hollander, W. M.: Personal communication.

Supplied: Tablets, 5 mg. (yellow) and 10 mg. (blue); bottles of 100, 500 and 1000. Tablets, 20 mg. (peach-colored); bottles of 100 and 1000.

a/019040

CIBA
SUMMIT, N.J.

because
your allergic patients
need a lift
a new R_x . . .

Plimasin®

(tripelennamine hydrochloride and methyl-phenidylacetate CIBA)

new, mild stimulant
and antihistamine

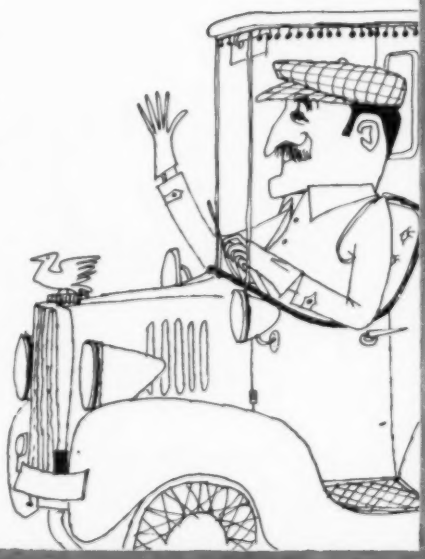
boost their spirits . . . relieve their allergic symptoms

So often the allergic patient is tired, irritable, depressed—mentally and physically debilitated. Frequently, antihistaminic agents themselves are sedative, adding to this already fatigued and disconsolate state.

Plimasin, because it combines a proved antihistamine with a new, mild psychomotor stimulant, overcomes depression and fatigue while it achieves *potent* antiallergic effects. Its new stimulant component —Ritalin—is totally different from amphetamine: smoother, gentler in action, devoid of pressor effect.

DOSAGE: *One or 2 tablets as required.*

Each Plimasin tablet contains 25 mg. Pyribenzamine® hydrochloride (tripelennamine hydrochloride CIBA) and 5.0 mg. Ritalin® (methyl-phenidylacetate CIBA).



C I B A SUMMIT, N. J.

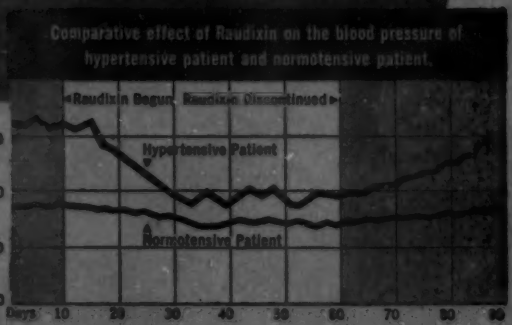
2/2191M

stable effect

RAUDIXIN

in anxiety and tension states . . .
stable therapeutic tranquilizing effect
without excessive sedation

in hypertension . . .
stable hypotensive effect without rapid peaks and
declines in blood pressure



The hypotensive action of Raudixin is selective for the hypertensive state. For this reason, Raudixin does not significantly affect the blood pressure of normotensive patients.

DOSAGE: 100 mg. b.i.d. initially; may be adjusted within a range of 50 mg. to 500 mg. daily. Most patients can be adequately maintained on 100 mg. to 200 mg. daily.

SUPPLY: 50 mg. and 100 mg. tablets, bottles of 100, 1000 and 5000.

SQUIBB

"RAUDIXIN"® IS A SQUIBB TRADEMARK